Corporate Presentation

Immune Responses, On Cue™

Nasdaq: CUE

March 2022

CUE™
BIOPHARMA

Forward-Looking Statements Disclosure

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Cue Biopharma's Vision

Leading the next wave of disruptive, breakthrough immunotherapies addressing the specificity and diversity of the human immune system to cure complex human disease.

- Harnessing natural signals ("Nature's Cues") for tailored immune activation against cancers to enhance efficacy and tolerability
- Enabled by rational protein engineering to design therapeutics with potentially enhanced selectivity and activity
- Emerging clinical data, including clinical response and patient benefit, provides potential for de-risking and validation of the ***entire*** platform
- Platform modularity and scalability expected to support versatile clinical applications and enhanced efficiencies in manufacturing and cost

Immunotherapy Has Transformed Oncology Treatment

Checkpoint inhibitors provided early insights that immunotherapy has the potential to eradicate cancer, however many challenges remain

- Overall response rates for checkpoints are 15-25%, depending on tumor type
- Many tumors show an absence of T cell infiltration i.e., many tumors are “cold”

How do we make immunotherapy more effective?

Increasing and activating tumor targeted T cells is key to enhancing therapeutic benefit

- IL-2 was the first cytokine to be successfully used in the treatment of cancer because it promotes expansion, function and survival of effector T cells
- IL-2 was approved for therapy of metastatic melanoma and metastatic renal cell carcinoma
- Overall response rates have remained low due to narrow therapeutic window and poor tolerability

The major challenge in the development of IL-2 as a therapeutic antitumor agent is that IL-2 acts indiscriminately on all T cells – leading to severe toxicity

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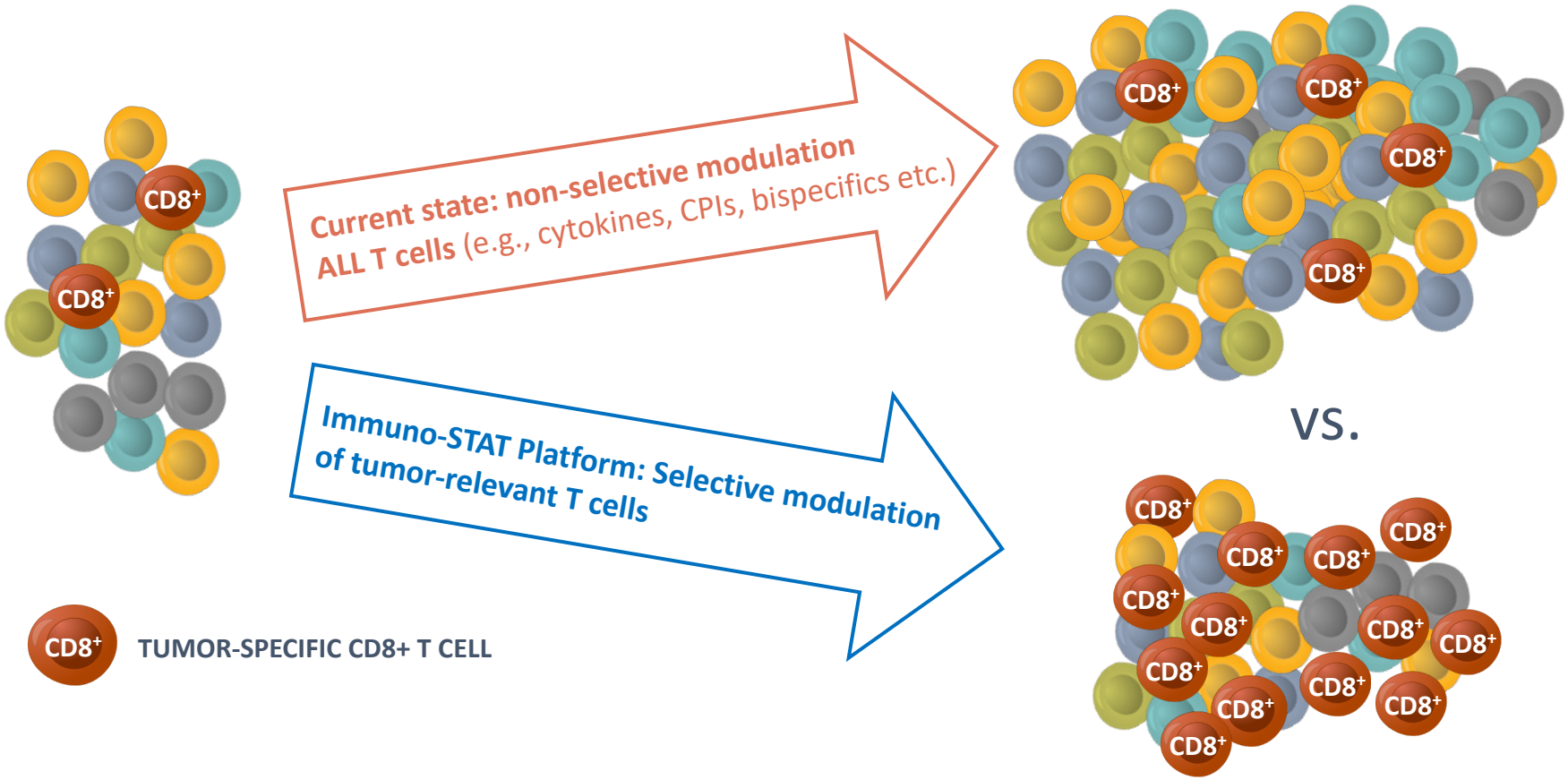
Successful Cancer Immunotherapy: Need for Selective Increase of Cancer-specific Cytotoxic T cells in the Tumor

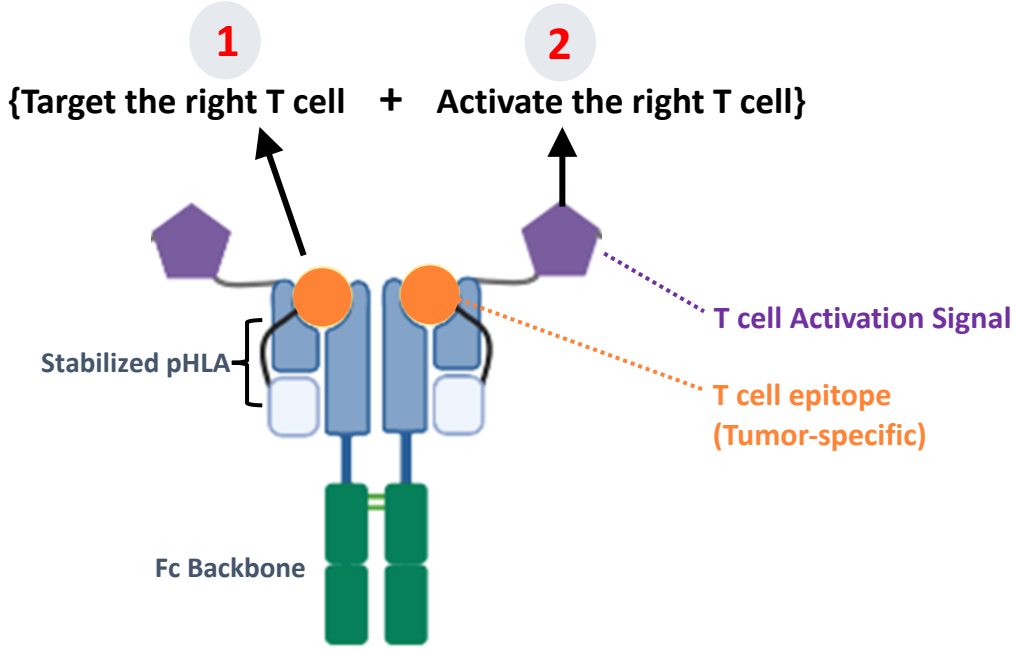
A minute fraction of a patient's baseline T cell repertoire (likely < 0.1%) is tumor-specific



- Limited Efficacy
- Lack of Selectivity
- Poor tolerability
- **Sub-optimal Patient Outcomes**

- Potential for greater efficacy
- Specific and selective
- Well tolerated
- **Enhanced Patient Outcomes**

Immuno-STATs: Designed to Selectively Increase the Number of ***Cancer-specific*** Cytotoxic T cells in the Tumor



Immuno-STAT Design

- **Single biologic molecule**
- **Ab-like manufacturability and CMC**
- **Stable, off-the-shelf**
- **IV (or SC) administration**

Manufacturable

- Ab-based modular design
- Ab-like manufacturability and CMC
- Highly stable (> 3-year stability)

Selective

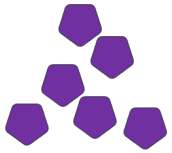
- Selectively activates tumor-specific T cells
- HLA specific
- No systemic immune activation

Clinically Active

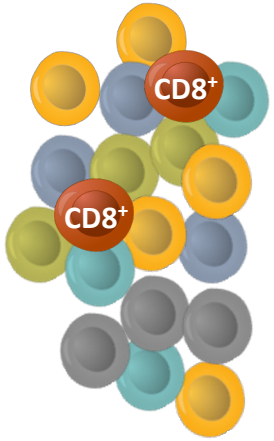
- Foundational preclinical data
- Emerging clinical activity with supporting PD
- Able to target diverse set of tumor antigens

IL-2: Indiscriminate Activation = Lack of Therapeutic Index

Wild Type IL-2 or IL-2 Variants

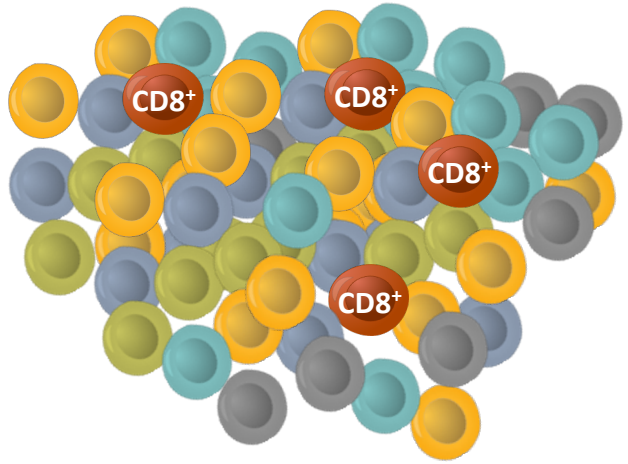


Lack of Selectivity for Tumor-specific CD8+ T cells



CD8+ TUMOR-SPECIFIC CD8+ T CELL

Non-selective Activation of CD8+ T cells



Examples

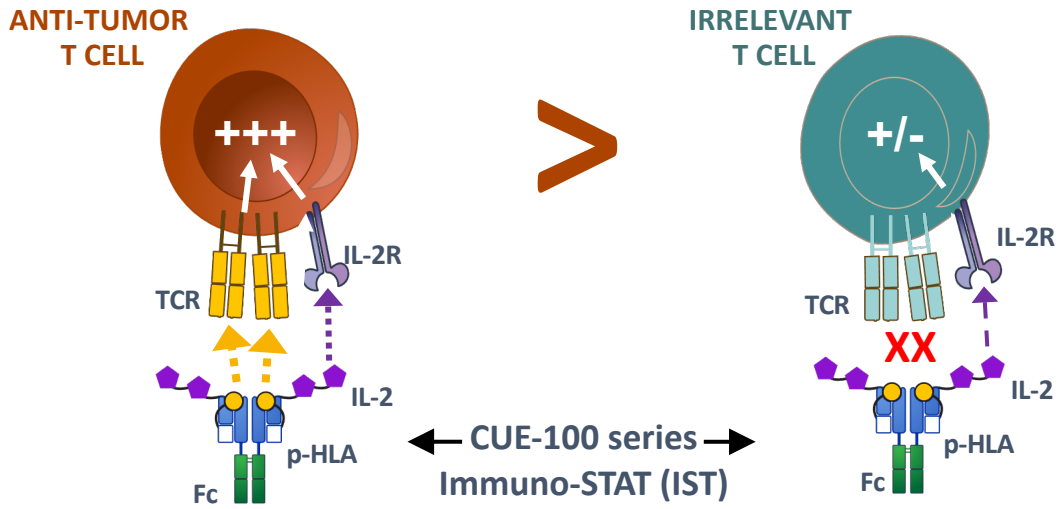
- **WT IL-2** (aldesleukin)
- **"Not-alpha" IL-2 variants** (e.g., NKTR-214)
- **Tumor-localized IL-2 variants** (e.g., FAP-targeted)
- **"Masked" IL-2 for conditional activation**
- **Lineage-biased IL-2 variants** (e.g., CD8+ T cells, or PD-1+ T cells)

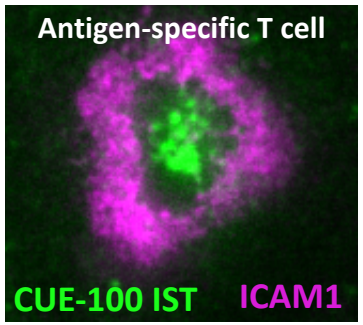
Considerations and Challenges

- **No selectivity for tumor-specific T cells**
- **Indiscriminate activation**
- **Activation of Tregs**
- **Toxicities (VLS, CRS etc.)**

CUE-100 Series Immuno-STATs: Enabling a Therapeutic Index for IL-2

Exploiting TCR and IL-2 co-engagement to selectively activate tumor-specific T cells

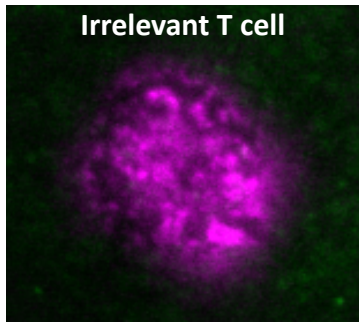




LAB OF DR. MICHAEL DUSTIN

UNIVERSITY OF OXFORD

CUE 100 series ISTs form functional Immune Synapses with Ag-specific T cells



CUE-100 series is an innovative modality targeting IL-2 directly to anti-tumor T cells

Lead candidate CUE-101 dosed up to 8.0 mg/kg with no MTD

vs.

Other IL-2 modalities *do not* selectively target anti-tumor T cells

- ***WT IL-2*** *(aldesleukin)**
- ***"Not-alpha" IL-2 variants*** *(e.g., NKTR-214)**
- ***Tumor-localized IL-2 variants*** *(e.g., FAP-targeted)*
- ***"Masked" IL-2 for conditional activation***
- ***Lineage-biased IL-2 variants*** *(e.g., CD8+ T cells, or PD-1+ T cells)*

*** Range of tolerated clinical doses: 0.006 – 0.04 mg/kg**

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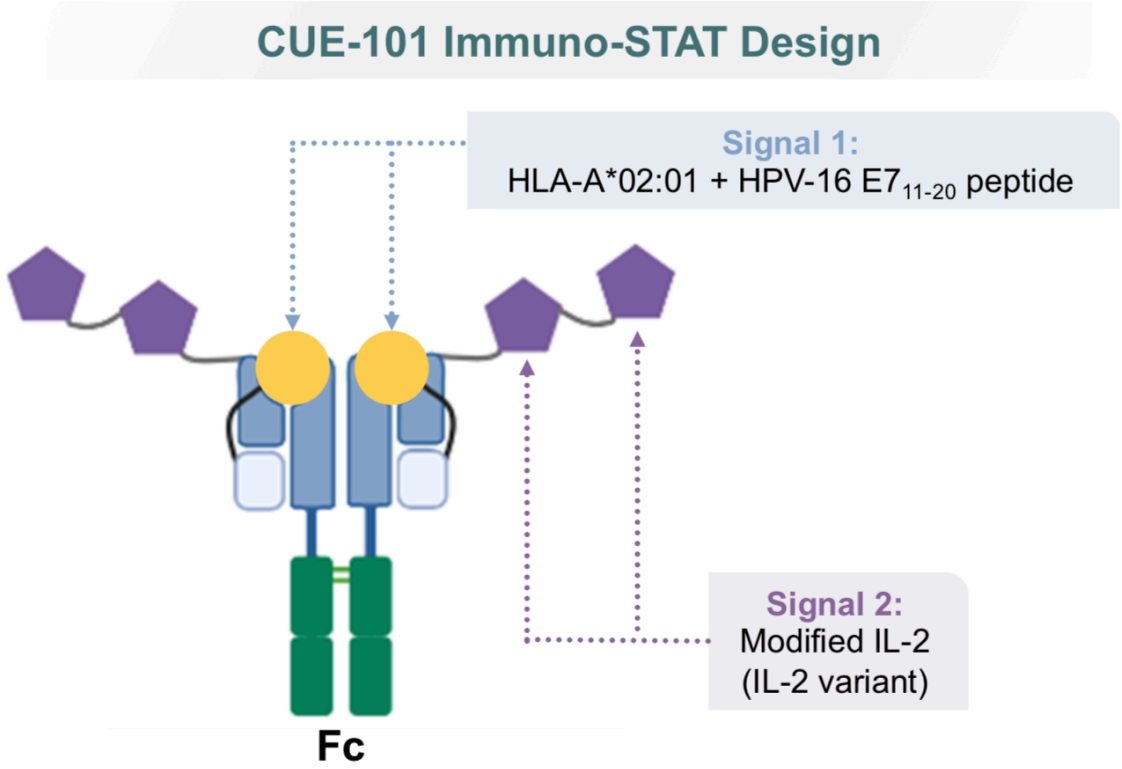
CUE-101: Lead Clinical Candidate Designed to Selectively Prime and Expand HPV E7-Specific T cells



- HPV induces several epithelial cancers including a significantly increasing fraction of head and neck cancer
- HPV-16 E7 is a viral proto-oncogene and contains a highly conserved and immunogenic T cell epitope (E7$_{11-20}$) presented by HLA-A02:01
- CUE-101 clinical development builds upon robust preclinical data[1] and patient stratification[2]

1: Quayle et al., *Clin Cancer Res* Jan 2020 DOI: 10.1158/1078-0432.CCR-19-3354
2: Patients must be HLA:02:01 and HPV-16+

CUE-101 is a "Beachhead" that Provides Clinical PoC and Platform De-risking

CUE-101 has been dosed in >50 patients

- Demonstrates anti-tumor activity both as a monotherapy in 3L r/m HNSCC patients, and in combination with KEYTRUDA® *(pembrolizumab, Merck's anti-PD-1 therapy)* in 1L r/m HNSCC

Highlights of Clinical de-risking data

- Safety and tolerability ***(dosed from 0.06 mg/kg up to 8.0 mg/kg; no MTD)***
- Sustained exposure upon repeated dosing ***(no evidence of drug-clearing ADAs)***
- Therapeutic window of drug dosing ***(1mg/kg – 4mg/kg)***
- Clinical metrics of anti-tumor activity ***(confirmed PRs and SDs per RECIST 1.1 criteria)***
- De-risking of the core CUE-100 series platform

Registration path opportunities for both mono- and combo-therapy in 3L and 1L r/m HNSCC, respectively

- Team preparing for initial discussion with FDA in 2H 2022 to discuss monotherapy RP2D data and defining next steps for potential registration path

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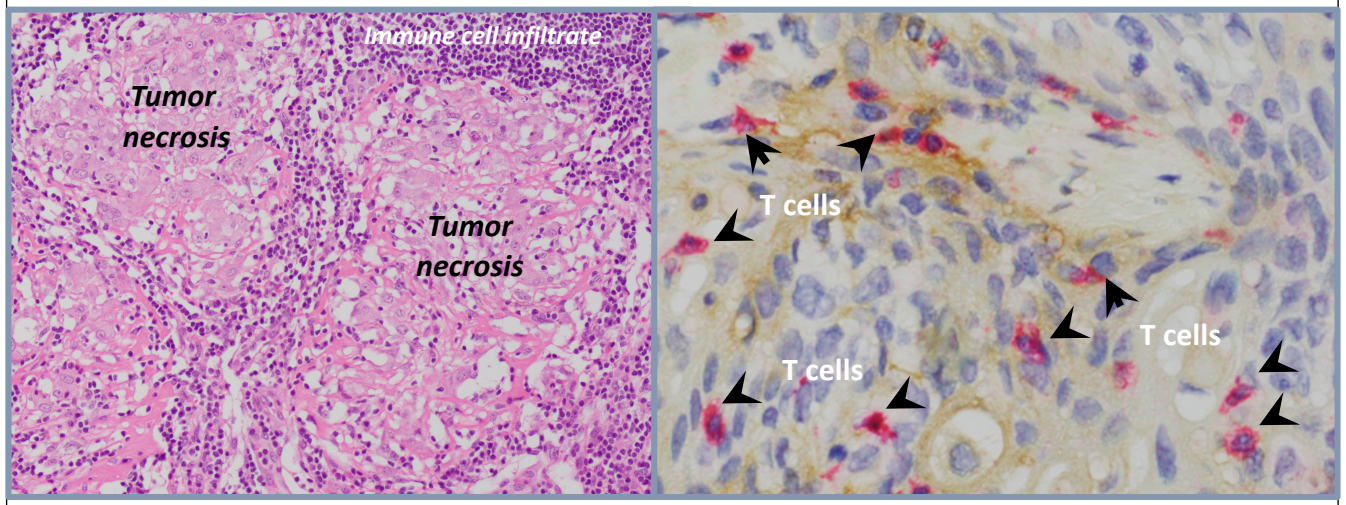
CUE-101 Monotherapy: Patient Tumor Biopsies Reveal Evidence of T cell Infiltration and Tumor Necrosis

Patient Example (1mg/kg):
Tumor Necrosis and T cell Infiltration on Treatment with CUE-101

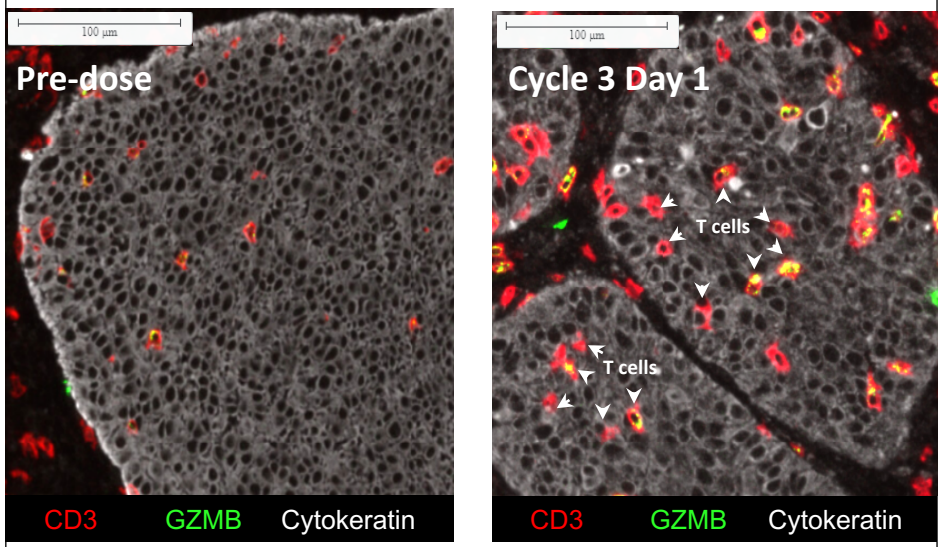


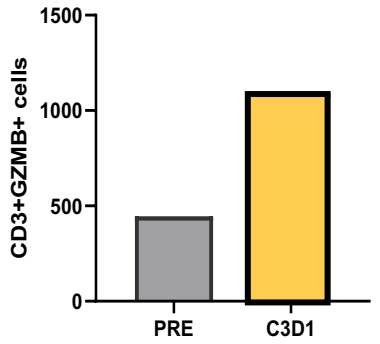
Case History

- Prior therapy – 1L chemotherapy and 2L pembrolizumab
- Progressive disease prior to enrollment
- Confirmed and sustained SD through 18 weeks
- Target lesion resected at 18 weeks due to proximity to an artery

Patient remains disease free post resection

Patient Example (2mg/kg):
Activated T cell Infiltration in Tumor pre- vs. post-CUE-101





Case History

- Prior therapy: 1L chemotherapy and 2L pembrolizumab
- Progressive disease prior to enrollment

CUE-101-01 Response/Durable Stable Disease (RP2D 4 mg/kg N = 16/18 patients evaluable for Response)

Responses	N	%
Objective Response *(CR or PR confirmed ≥ 4 weeks)*	1	6.3%
Durable Stable Disease *(SD sustained for ≥ 12 weeks*)*	6	37.5%
Clinical Benefit *(CR/PR + durable SD)*	7	43.8%

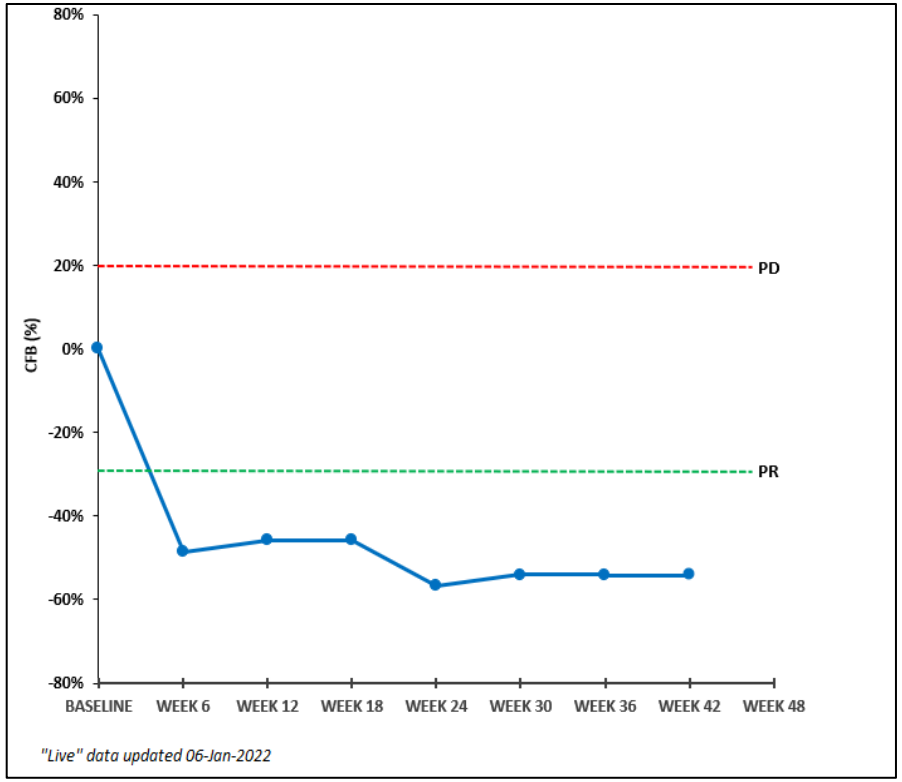
**Requires SD at ≥ 2 consecutive scans at 6-week and 12-week visits. Week 12 scans acquired during the 11th week are permitted. Based on RECIST 1.1 radiologic SD*

CUE-101: Confirmed PR in Monotherapy with Supporting PD Metrics

Case History

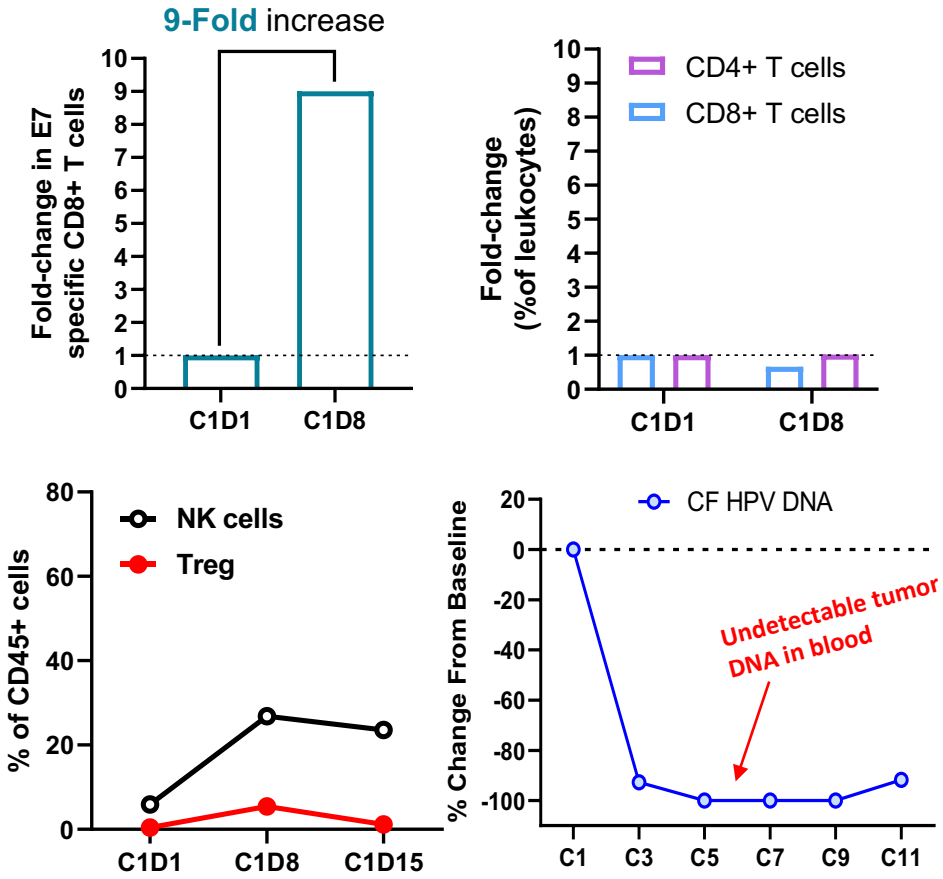
- Prior therapy:
  - 1L cetuximab
  - 2L pembrolizumab
- Progressive disease prior to enrollment
- Treated in metastatic 3L setting with 4.0 mg/kg CUE-101 Q3W (Cohort 6)
- Patient completed 14 cycles of CUE-101

Change from Baseline (CFB) in Sum of Diameters of Target Lesion(s)

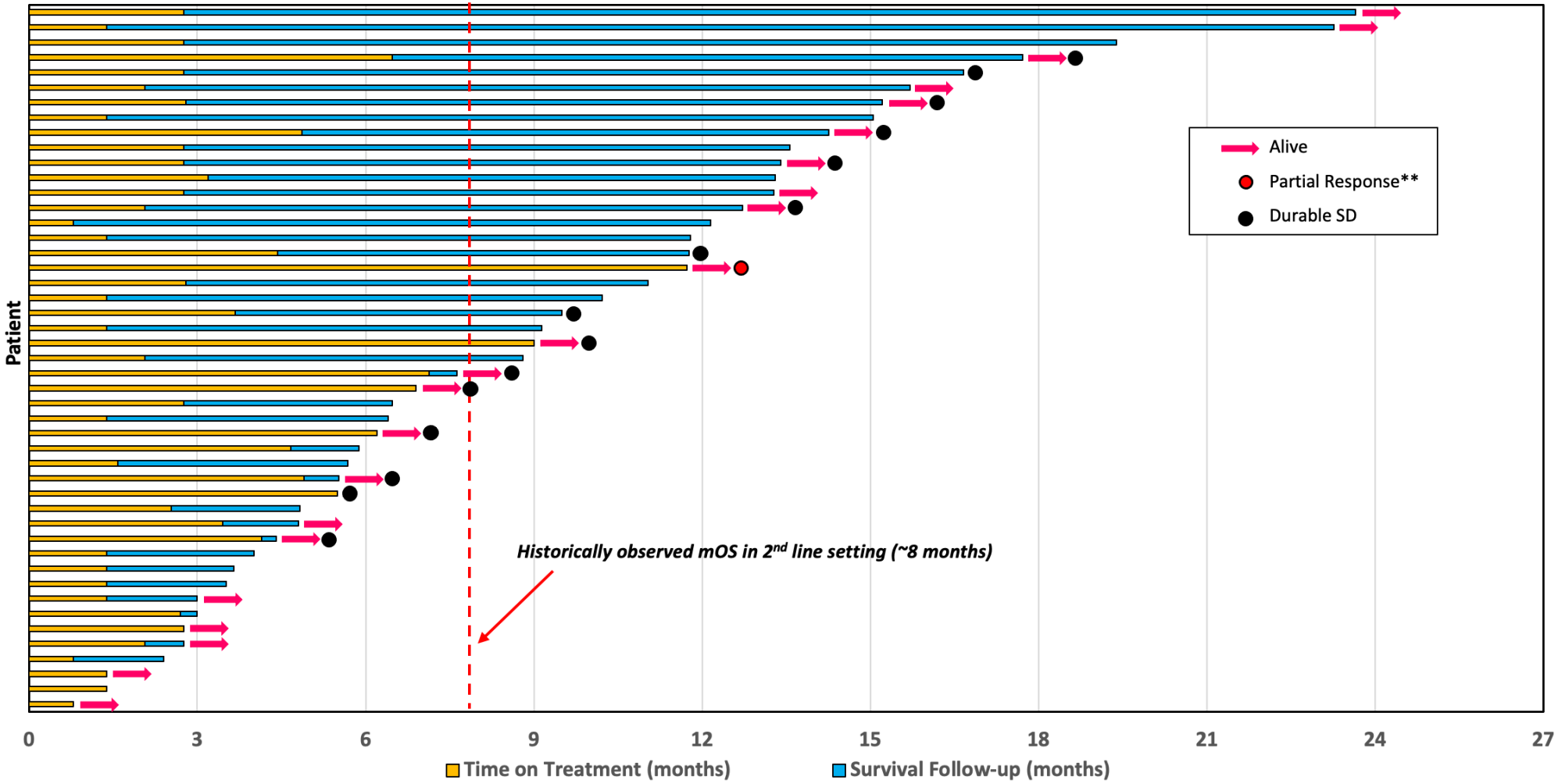


- Confirmed PR
- Duration of Response 42 weeks

Increase in HPV E7-specific CD8+ T cells with minimal change in total T cells



Overall Survival: Monotherapy Patients Across All Cohorts



** *Response symbols indicate patient experienced PR or Durable SD during the study. Onset and duration of the response is not indicated on the plot.*

CUE-101: Dose Escalation in Combination with Pembrolizumab

Pembrolizumab Combination Dose Escalation

Pembrolizumab 200 mg, Q3W	CUE-101 Dose (mg/kg)
	4.0
	2.0
	1.0

Cohort 3 → *Enrolling*

Cohort 2 → *Dosing complete, no DLTs*

Cohort 1 → *Dosing complete, no DLTs*

Cohort 1

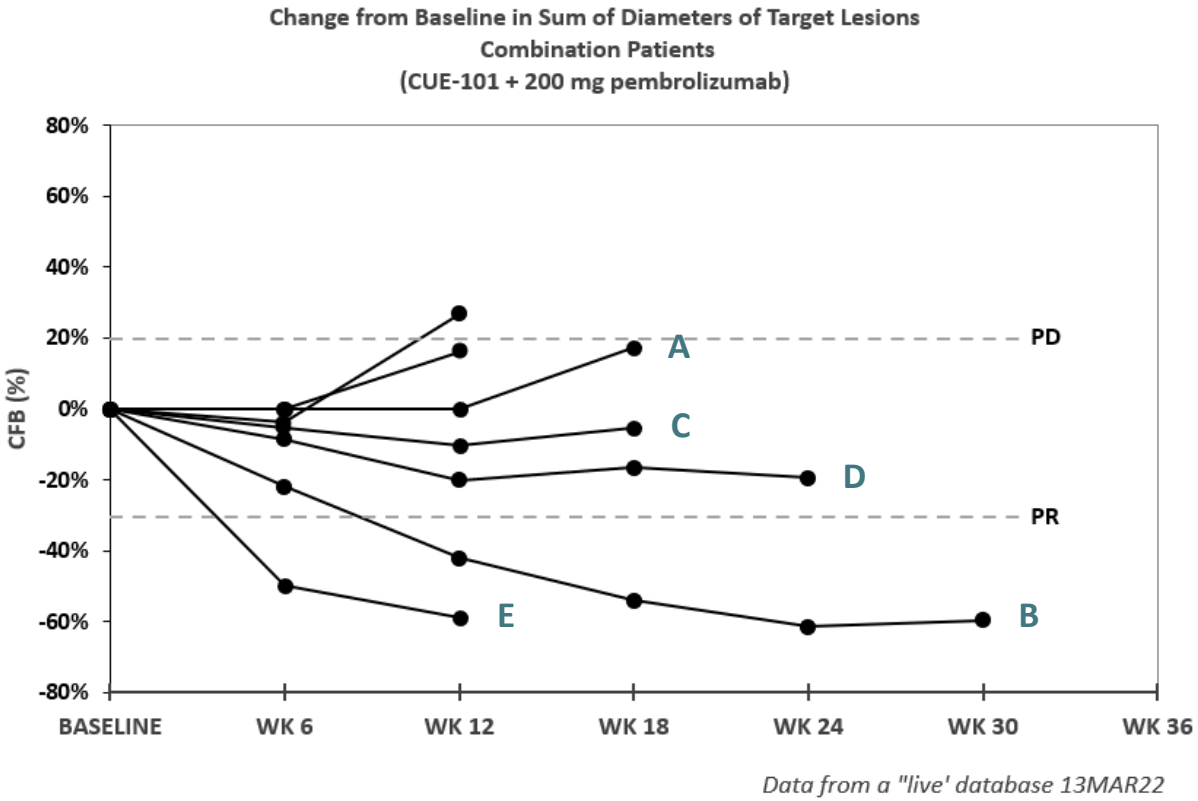
- 1 patient with durable SD (off treatment) **(A)**
- 2 patients with PD at week 12 (off treatment)

Cohort 2

- 1 patient with confirmed ongoing PR (remains on treatment) **(B)**
- 1 patient with durable SD (off treatment) **(C)**
- 1 patient with PD at week 6 (progression in non-target lesions) with reduction in target lesions (off treatment) **(D)**

Cohort 3:

- 1 patient with confirmed ongoing PR (remains on treatment) **(E)**
- 2nd patient enrolled 14-FEB-22 (remains on treatment)

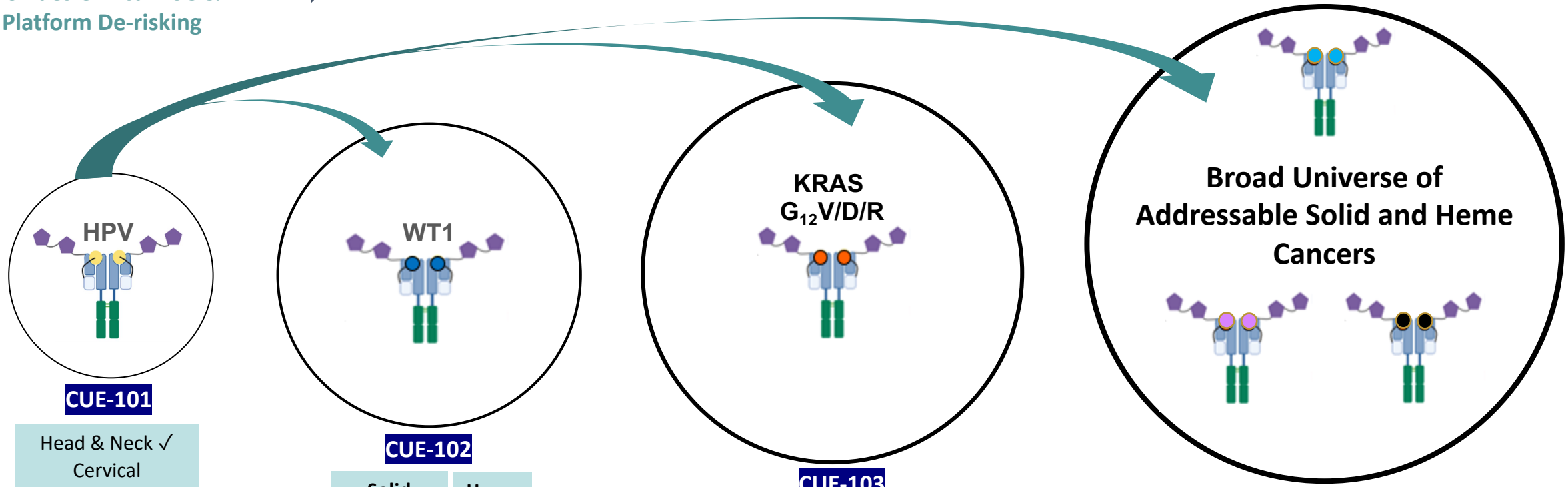


Data from a "live' database 13MAR22

Clinical PoC with CUE-101 Provides a Springboard for Expansion into Large Indications with Unmet Need

CUE-101 in r/m HNSCCC provides Clinical PoC & Platform De-risking

Rapid Expansion into Broad Indications with Significant Unmet Need



CUE-101

Head & Neck ✓
Cervical
Anal
Vulvar
Penile

CUE-102

Solid	Heme
CRC	AML
Gastric	ALL
Lung	MM
Ovarian	MDS
Pancreatic	
Breast	

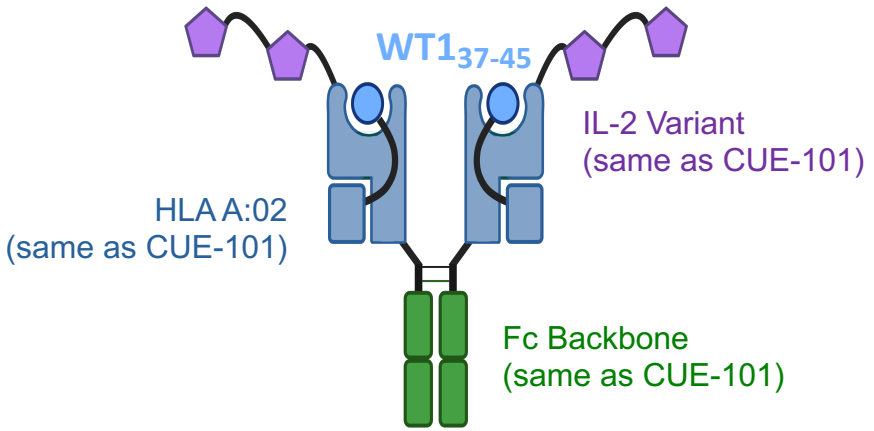
CUE-103

Pancreatic
CRC
Lung

TBD: CUE-104, CUE-105, CUE-106….

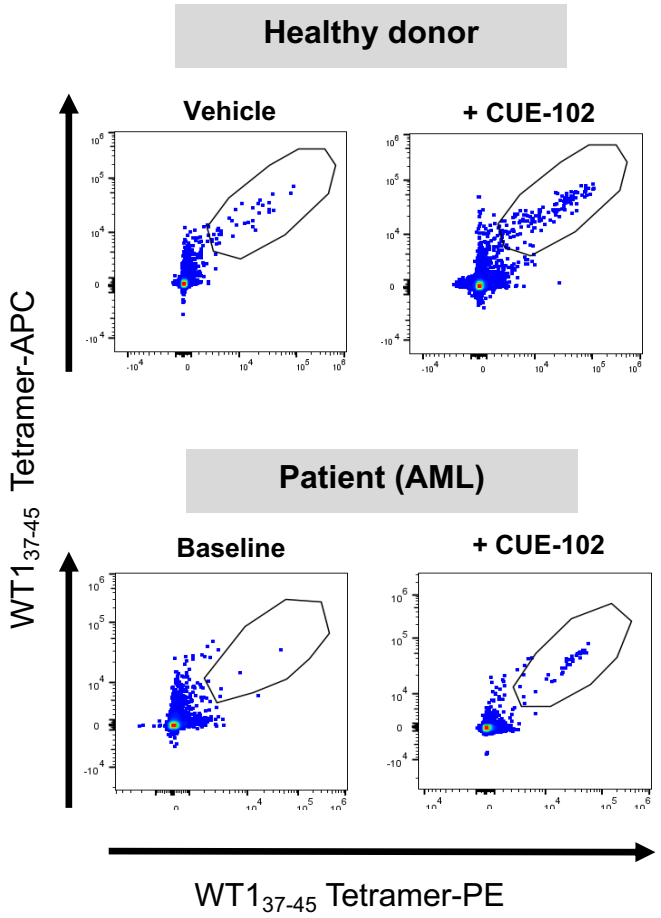
CUE-102: Wilms Tumor 1 (WT1) – IND on Track for 1Q 2022 Filing

Molecular Design
(99% sequence identity to CUE-101)

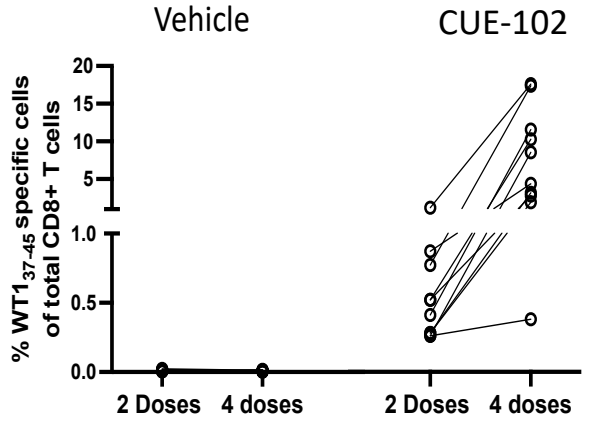


- **WT1 is the top-ranked onco-fetal tumor antigen by the NCI with restricted tissue-expression**
- **Core IL-2 framework is de-risked by the clinical experience of CUE-101**
- **Broad therapeutic opportunity in numerous solid (e.g., NSCLC, CRC, Pancreatic, Ovarian, Breast) and hematological cancers (e.g., AML, MM, ALL)**

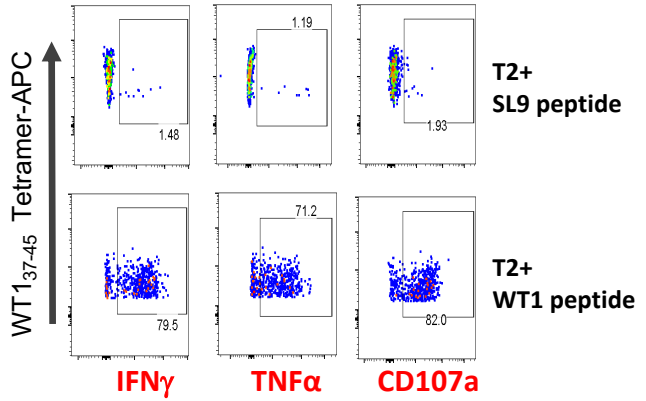
T cell expansion from healthy subject and AML patient



In vivo expansion of WT1 T cells (in HLA-A02 transgenic mice

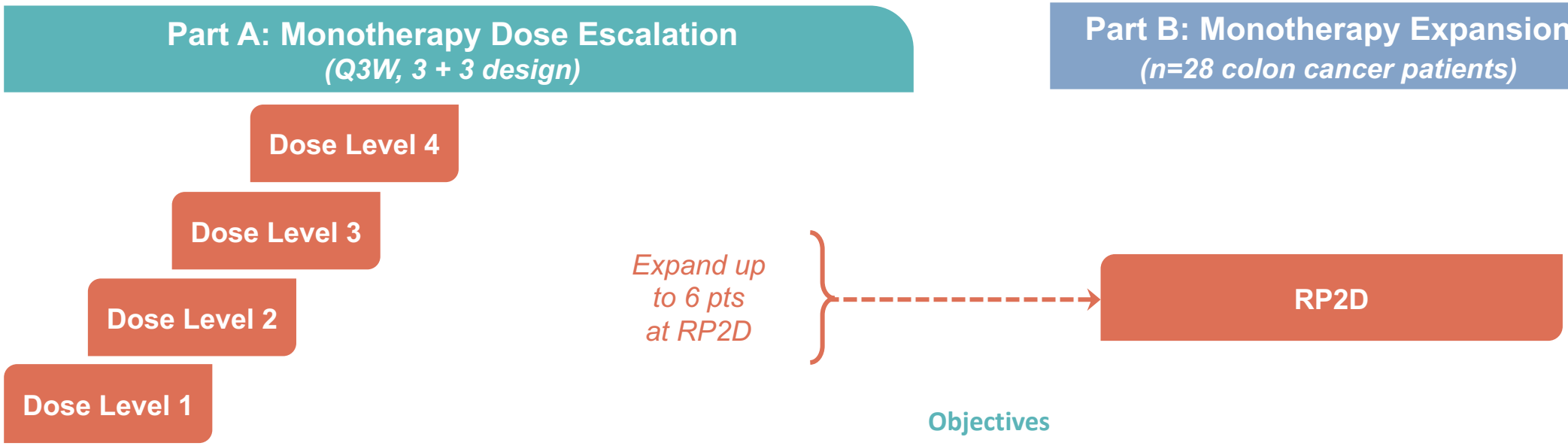


Polyfunctionality of CUE-102-expanded T cells



CUE-102: Monotherapy First-in-Human Phase 1 Trial

*CUE-102-01 is a Phase 1, FIH study to characterize the safety, tolerability, PK, PD, immunogenicity, and preliminary anti-tumor activity of CUE-102 in subjects who are HLA A*0201-positive, have WT1-positive, recurrent/metastatic cancers, and have failed conventional therapies.*



Eligibility

- WT1+ cancers (dose escalation: colon, gastric, pancreatic and ovarian; colon only for expansion)
- Measurable disease by RECIST 1.1
- HLA-A*0201 genotype

Objectives

- *Primary:* Safety and tolerability
- *Secondary:* PK, Anti-tumor activity (RECIST 1.1)

Biomarker (Pre/Post CUE-102 dose)

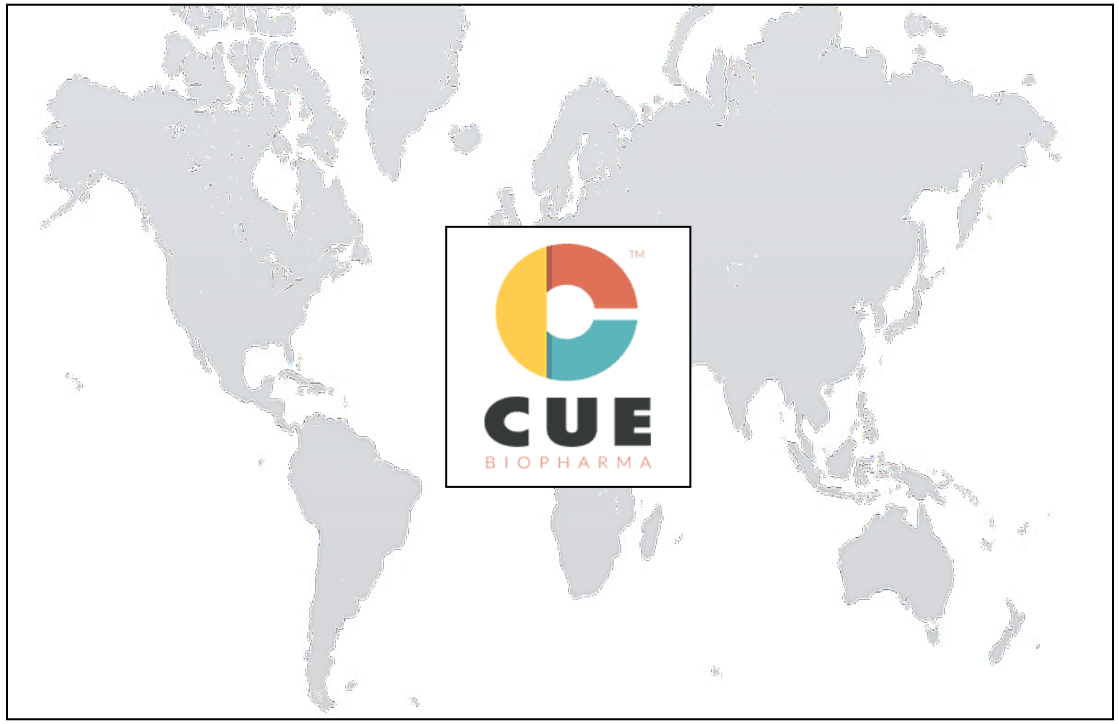
- WT1-specific CD8+ T cell counts and functionality
- Immunophenotyping, cytokine release, and TCR sequencing

Broad International IP Position

50+ Patent Families
Includes 4 in-licensed from the
Albert Einstein College of Medicine

80 Patents and 286 Pending Applications
Patents, PCTs and national filings cover
all aspects of Cue Biopharma's Immuno-STAT™
and other platforms

Patent Term for Cue Biopharma Products
Generic coverage through 6/35
Specific product coverage from 12/37 – 11/41



Applications include Australia, Brazil, Canada, China, EPO, Hong Kong, India, Israel, Japan, Korea, Singapore, Taiwan, and the US

Competitive Positioning and Differentiation

Recent clinical trial disappointments in the IL-2 space reinforce and support our premise that ***systemic, non-specific IL-2 administration with no selectivity for anti-tumor T cells*** will not provide a therapeutic index, nor demonstrable therapeutic benefit

Cue Biopharma's IL-2 based CUE-100 series ***selectively targets IL-2 to tumor-specific T cells via TCR specificity ("Nature's Cues"),*** demonstrating single agent therapeutic activity and potential for mechanistic synergy with checkpoint inhibitors

Capital Runway, 2022 Milestones and Use of Proceeds

Present cash runway into Q3, 2023

Focused and disciplined use of proceeds provides potential cash runway extension

CUE-101 (HPV HNSCC) exemplifies/de-risks/validates the IL-2 CUE-100 series:

- **CUE-101 Monotherapy trial evidencing single agent activity (potential registration path)**

  Define/determine single agent registration path to present to FDA 2H'22 regarding 3rd line therapy for patients who have failed chemotherapy and anti-PD1 regimens

- **Combination therapy with PD1 inhibition with potential for significant mechanistic synergy**

  First line HPV+ HNSCC in combination with pembrolizumab: initial readout by end of '22

CUE-102 *(WT1 expressing tumors)* IND filing end of Q1'22

Neo-STAT™ and RDI-STAT™ as next generation developments

CUE BIOPHARMA

Thank you

Rationally Engineered Biologics to Restore Immune Balance by Harnessing Nature's Cues for Selective and Specific Immune Modulation

CUE™ BIOPHARMA