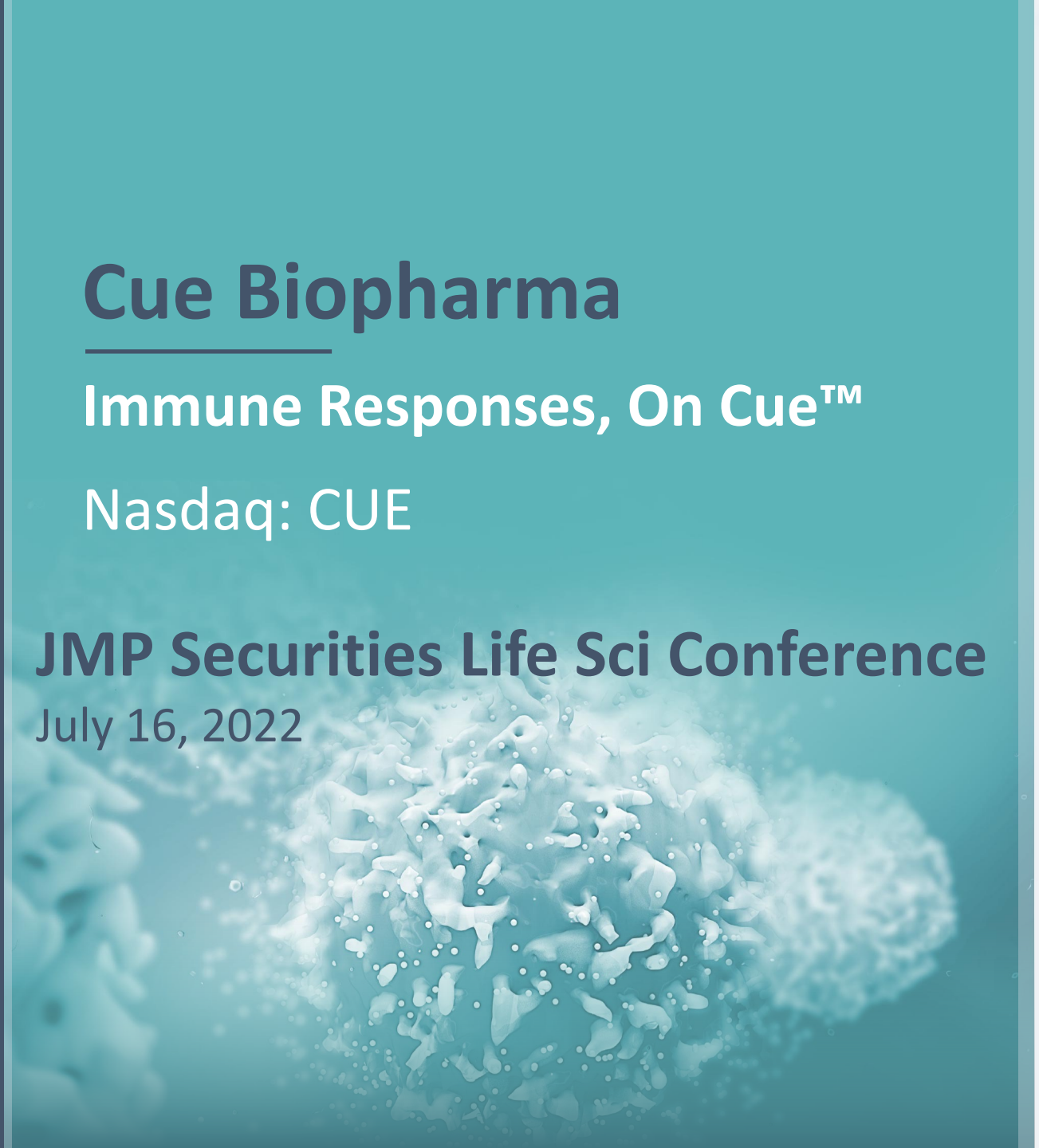
Cue Biopharma

Immune Responses, On Cue™

Nasdaq: CUE

JMP Securities Life Sci Conference

July 16, 2022



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Vision

Harness “Nature’s Cues” to deliver breakthrough therapies that activate a patient’s own immune system to attack cancer

Approach

- Rationally engineer and develop Immuno-STATs to selectively deliver activating signals to tumor-specific T cells
- De-risk and validate with positive tolerability and activity data from ongoing CUE-101 clinical studies
- Leverage modularity to address unmet patient needs across a broad range of cancers

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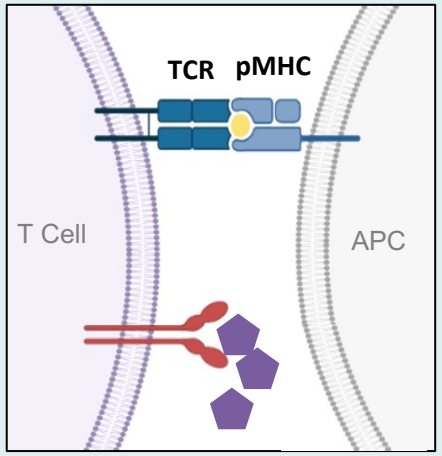
Immuno-STATs Enable Selective Immune Activation Against Cancer

Key Signals Driving an Immune Reaction

1: Antigen (Specificity)

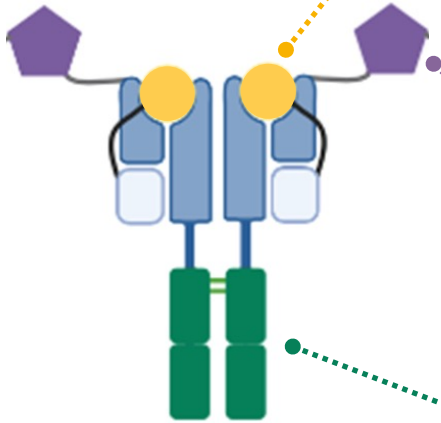
Antigen presenting cells display peptides that can be recognized by T cell receptors (TCR)



2: Co-stimulation (Modulation)

Once the TCR is engaged, cytokines and APC surface receptors determine T cell activation or tolerance

Immuno-STAT Design



Peptide Antigen in MHC

Peptide epitopes to target cancer-relevant T cells

Co-Stim/Co-Reg

Distinct biological signals, including cytokines and cell-surface receptors

Fc Backbone

Fc engineering to dial in or out biological and effector functions

Immuno-STATs unlock the full potential of cytokine therapy by leveraging antigen specificity to create a therapeutic window for activation of tumor-specific T cells that recognize and destroy cancers

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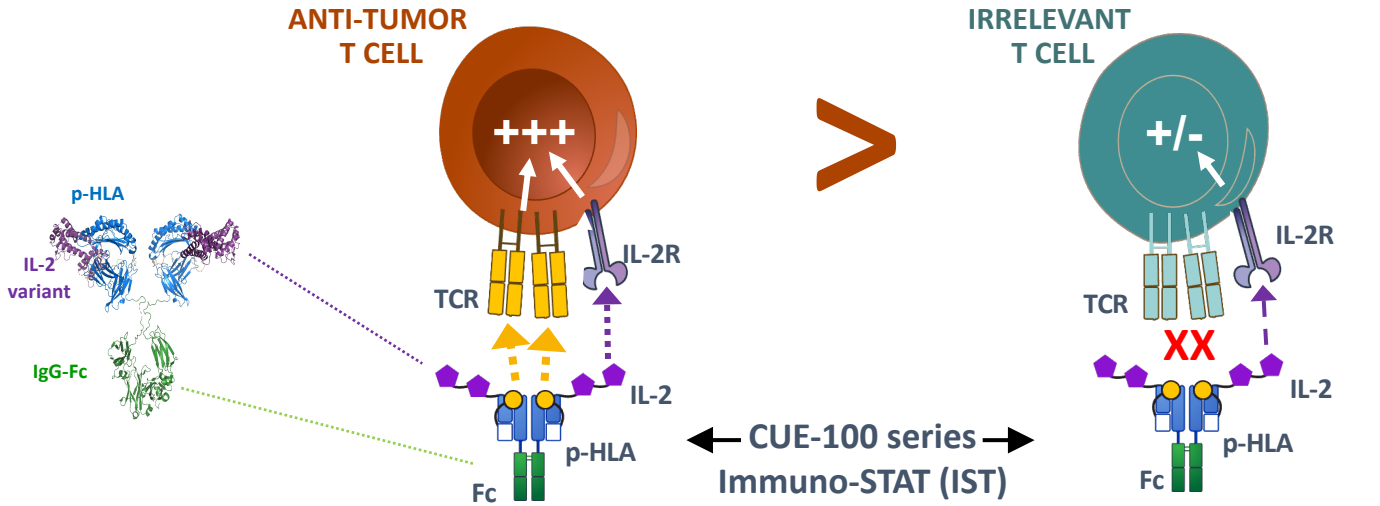
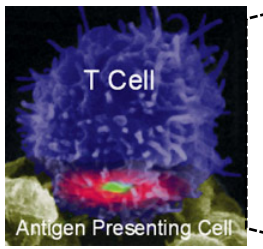
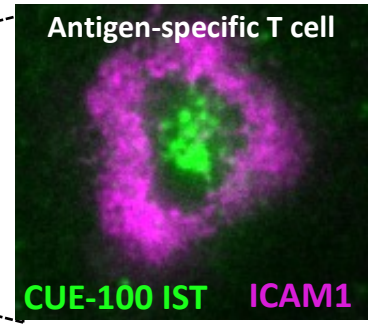
CUE-100 Series ISTs:
Tumor-specific T cell Engagers that Enable a Therapeutic Index for IL-2

TCR and IL-2R co-engagement results in selective activation of tumor-specific T cells





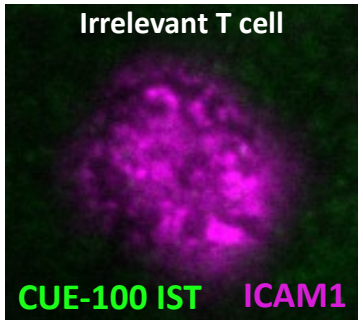
Immune Synapse



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

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

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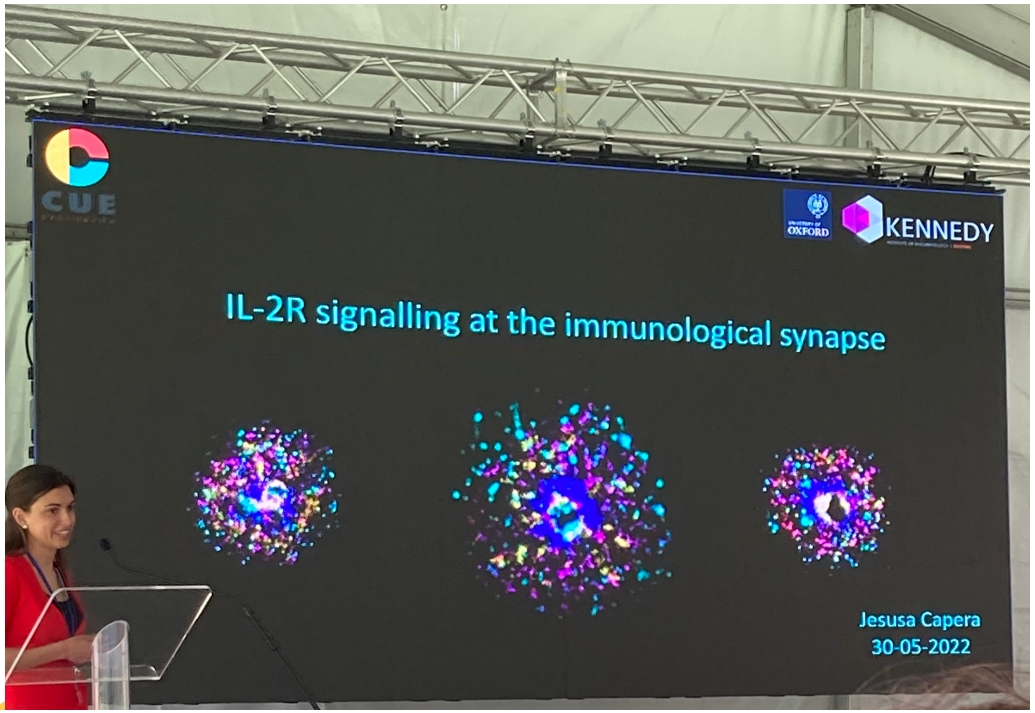
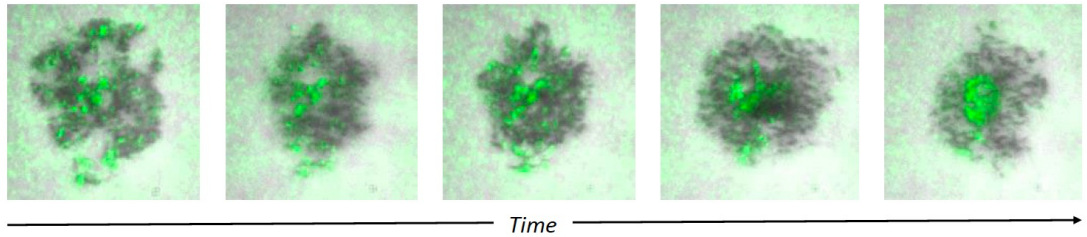
Immuno-STATs: TCR-selective engagers of anti-tumor T cells



Collaboration with Dr. Michael Dustin, Univ of Oxford

ImmunoSTATs Drive Synapse Formation and IL-2 Signaling

A.



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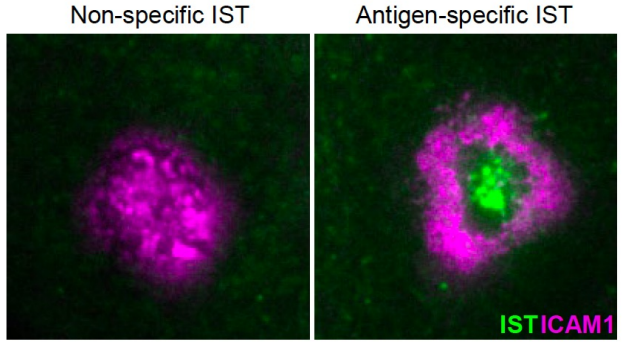

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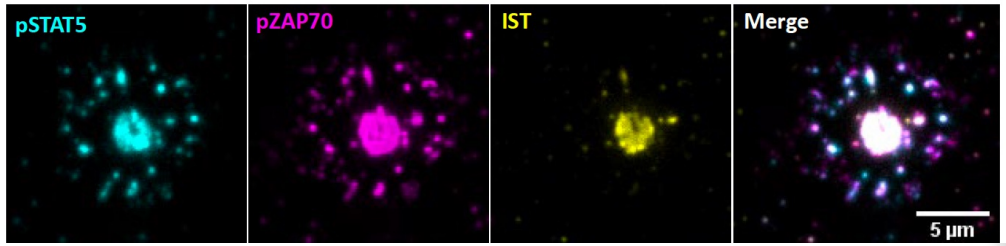
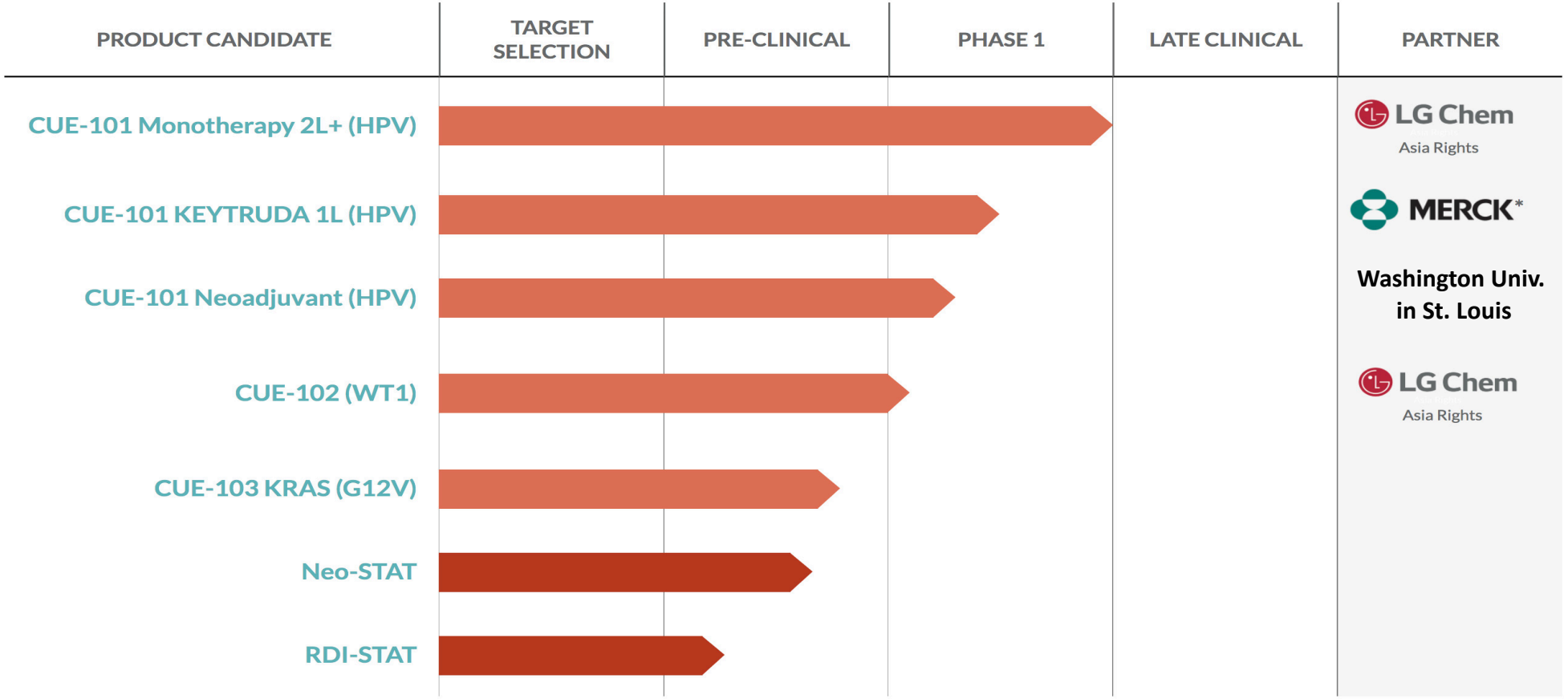


Evolving Immuno-Oncology Pipeline

IL-2 based CUE-100 Series and Derivatives



* CUE-101 Combo Trial with KEYTRUDA®

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CUE-101: Clinical Validation of a Novel Platform of T cell Engagers

Established a novel therapeutic platform for selectively activating tumor-specific T cells directly in patients

- Demonstration of safety and tolerability
- Demonstration of sustained drug exposure upon repeated dosing with no clinical evidence of immunogenicity
- Demonstration of selective expansion of tumor-specific immune cells
- Evidence of T cell infiltration into tumor and increased tumor necrosis
- Demonstration of single-agent anti-tumor efficacy
  - (*RECIST-based PR and SD in 3L+ R/M HNSCC patients*)
- Early evidence of enhanced activity in combination with CPI (confirmed PRs and SDs observed in dose escalation)

Platform de-risking expedites clinical development timelines and regulatory path for subsequent molecules

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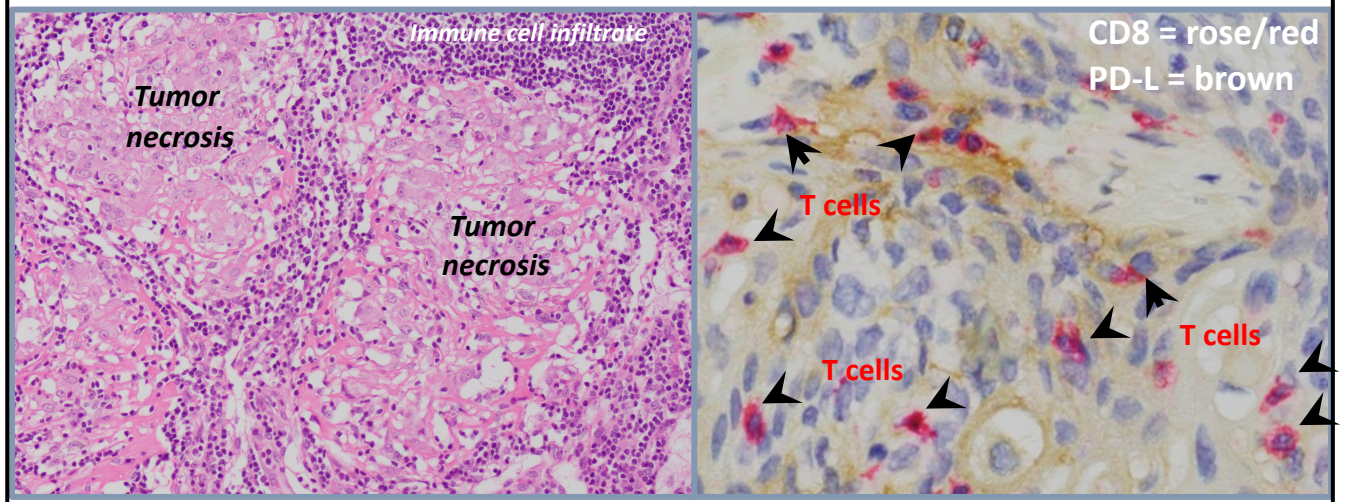
CUE-101: Monotherapy Patient Tumor Biopsies Reveal Evidence of T cell Infiltration and Tumor Necrosis

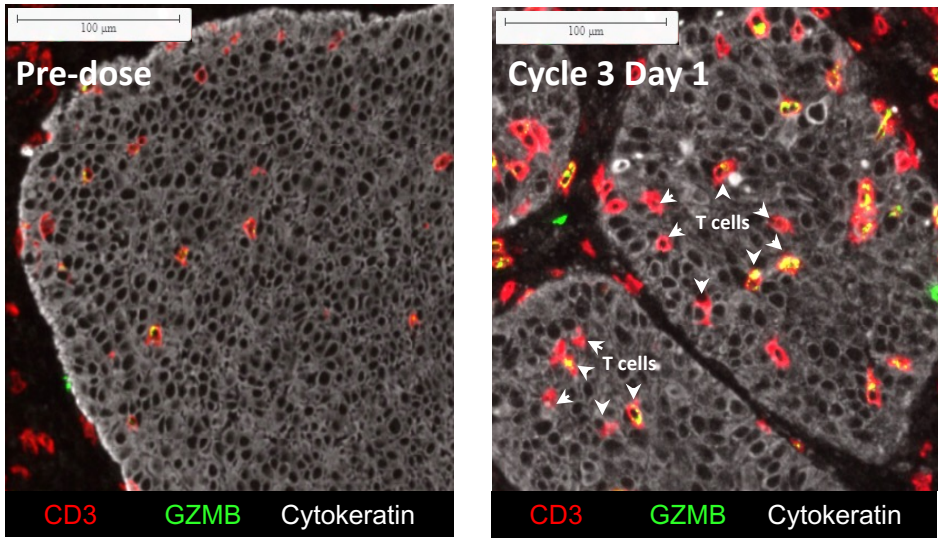
Patient A (1 mg/kg): Tumor Necrosis and T cell Infiltration on Treatment with CUE-101

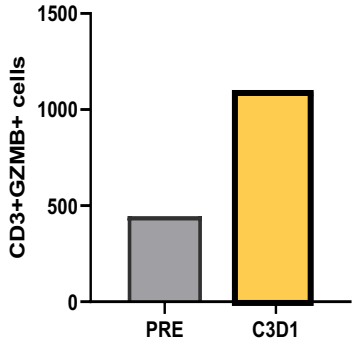


Case History

- 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 alive at 19.6 months**, no evidence of disease, no treatment since resection

Patient B (2 mg/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

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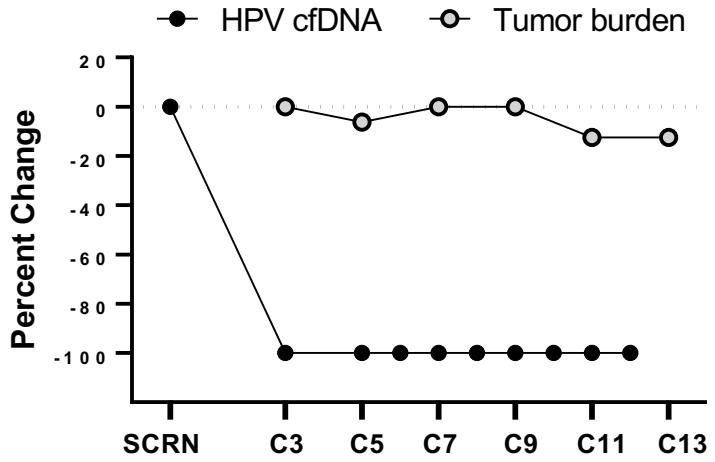
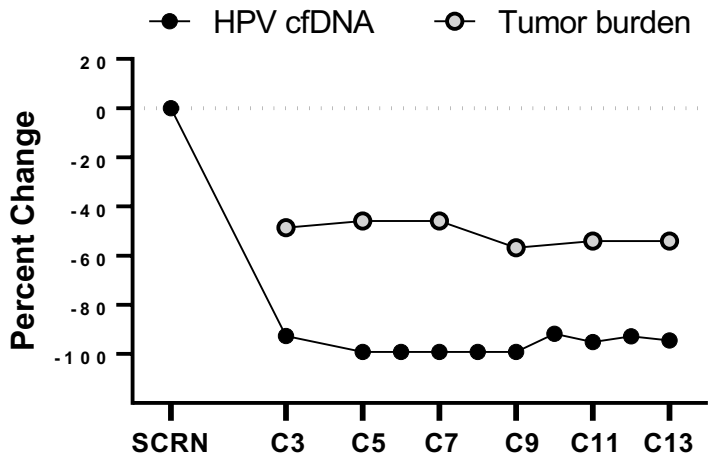
Correlation of HPV cfDNA and Tumor Burden

RECIST criteria may not reflect true disease status

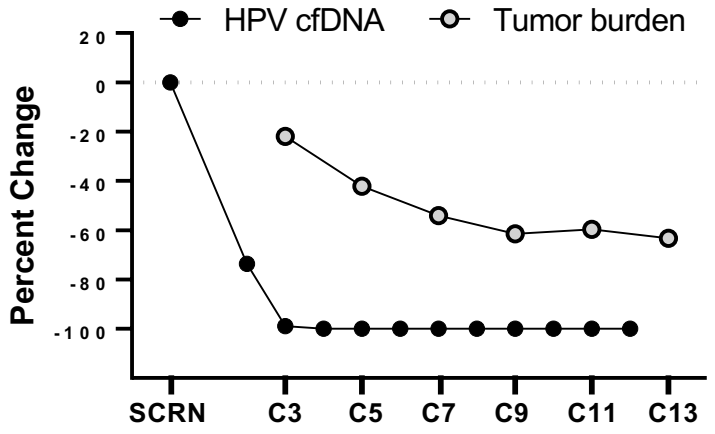
ID:XXX-004 (4 mg/kg CUE-101)



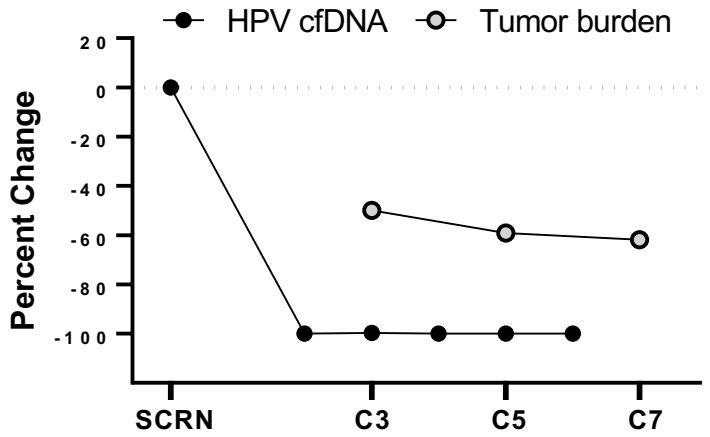
ID:XXX-018 (4 mg/kg CUE-101)



ID:XXX-020 (2 mg/kg CUE-101 + Pembro)



ID:XXX-024 (4 mg/kg CUE-101 + Pembro)



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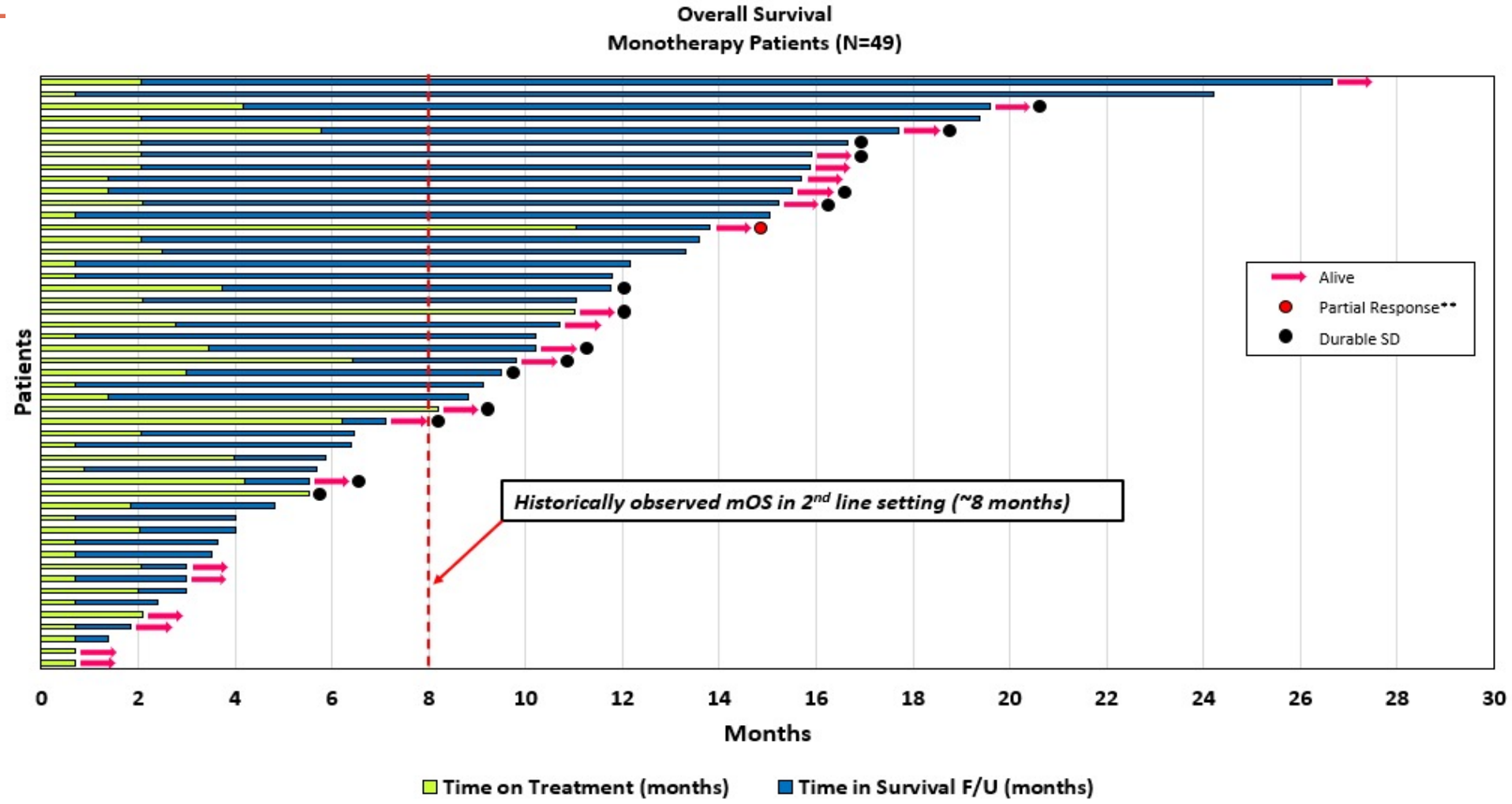
Overall Survival from Dose Escalation Monotherapy



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

Data cutoff April 2022

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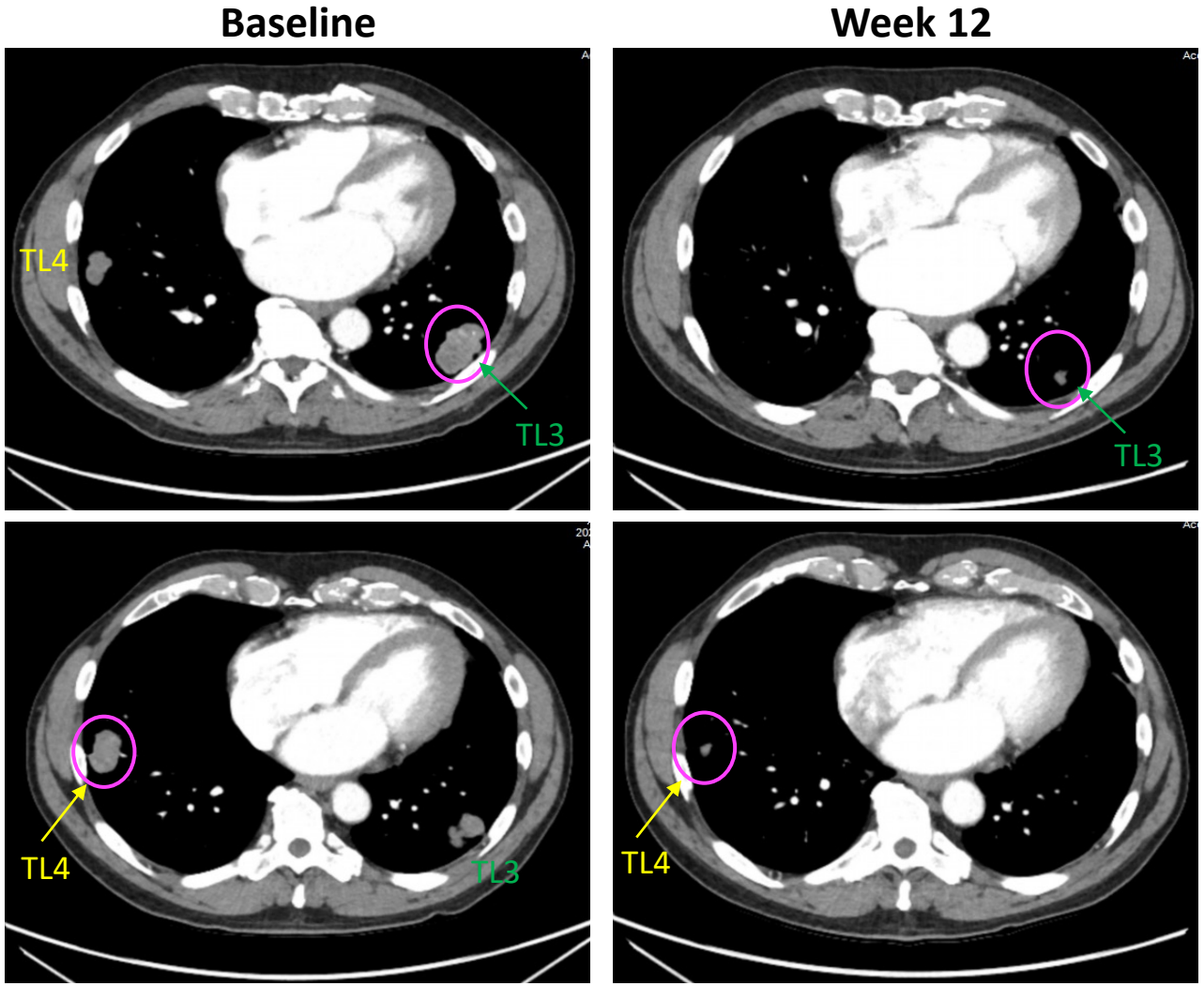
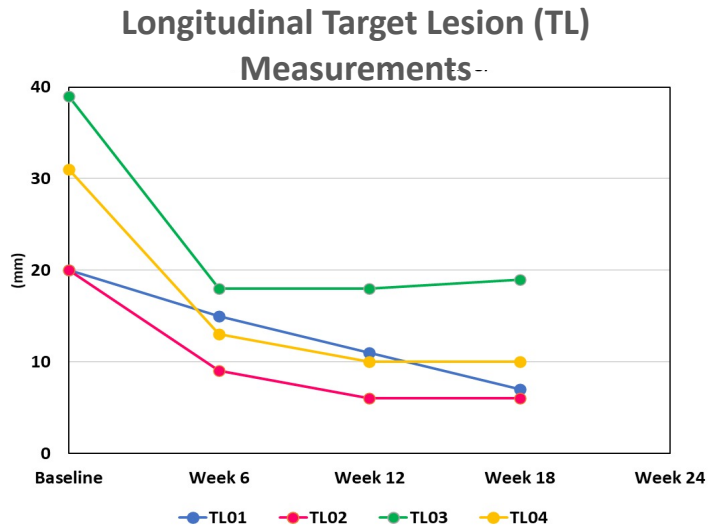
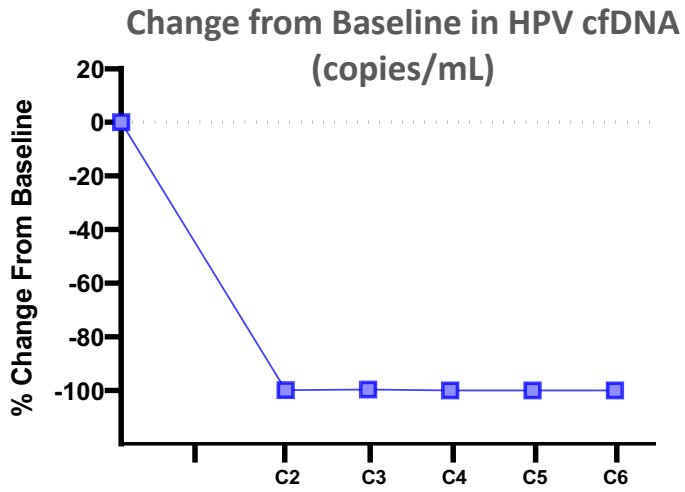
CUE-101: Confirmed PR in Combo Cohort 3 (4 mg/kg + pembrolizumab)







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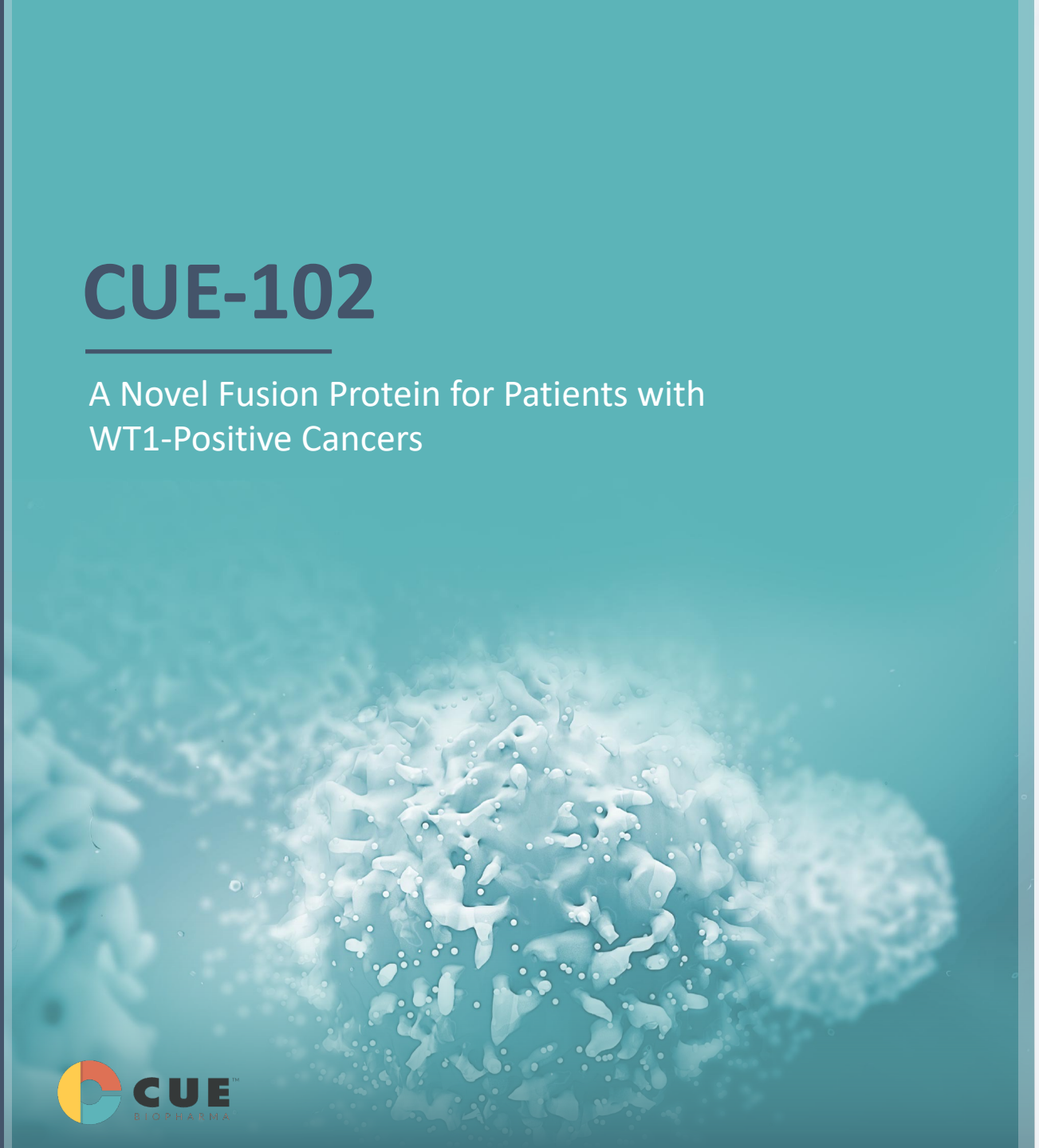
CUE-102

A Novel Fusion Protein for Patients with WT1-Positive Cancers



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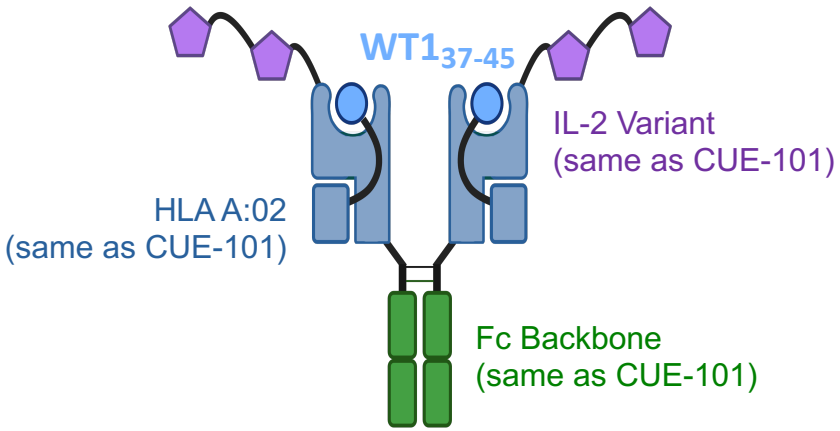
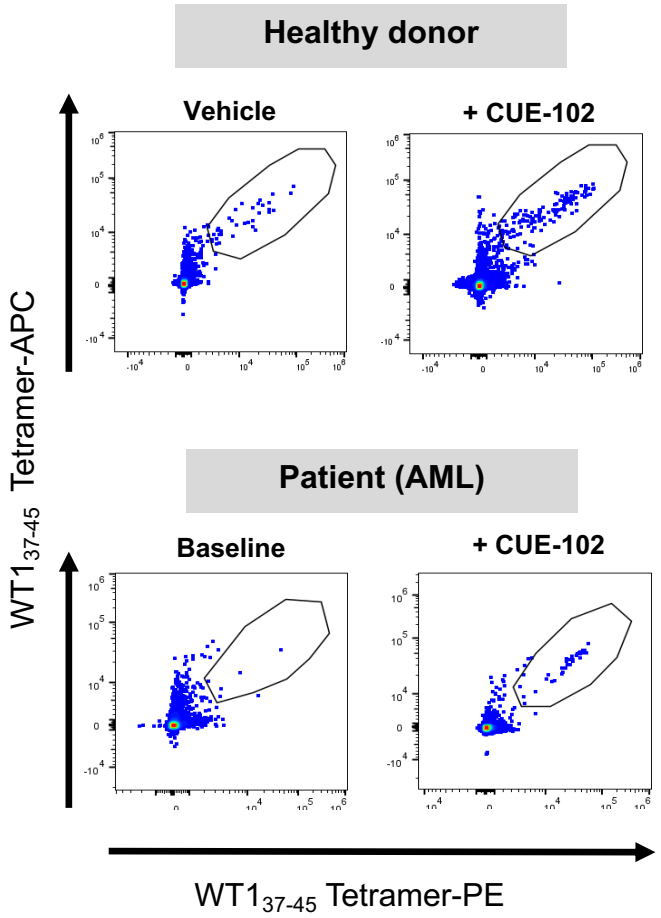
CUE-102: Wilms Tumor 1 (WT1)

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

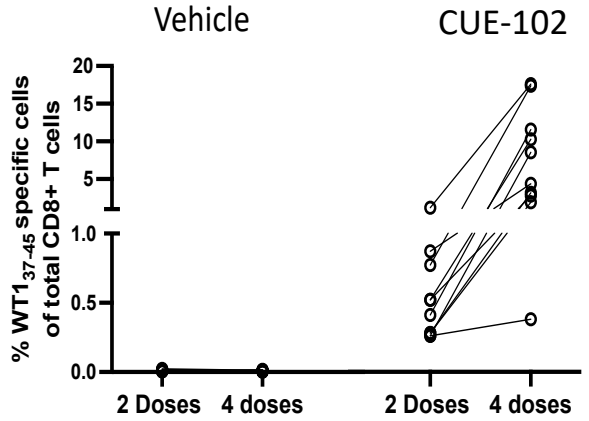


- **WT1 is the top-ranked onco-fetal tumor antigen by the NCI with restricted tissue-expression**
- **Core IL-2 framework is de-risked by the clinical experience of CUE-101**
- **Broad therapeutic opportunity in numerous solid (e.g., NSCLC, CRC, Pancreatic, Ovarian, Breast) and hematological cancers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

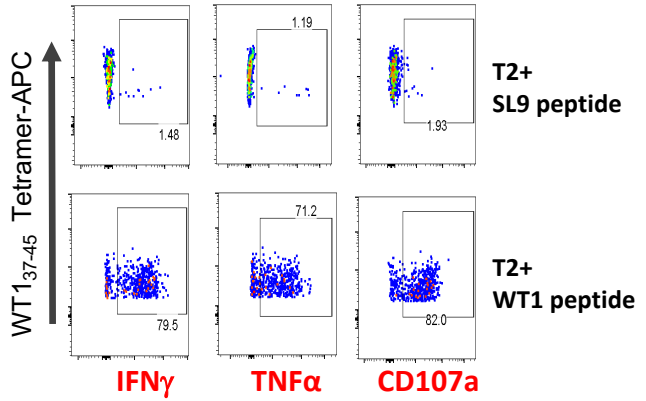
T cell expansion from healthy subject and AML patient



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



Polyfunctionality of CUE-102-expanded T cells



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CUE-102: Safe to Proceed Letter Received from FDA 29APR2022

- IND submission characterized CUE-102 pharmacology, demonstrated the MoA, and emphasized comparability and relevance of clinical experience with CUE-101

ADVANTAGES OF PLATFORM MODULARITY

- No additional nonclinical toxicology was required
- Approval to start with dose of 1 mg/kg *(~20-fold higher than CUE-101)* results in saving 8-9 months of clinical development time and cost

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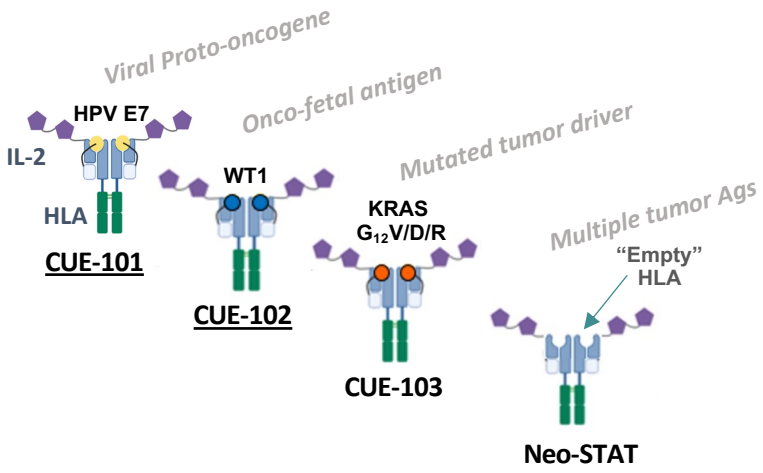
Vision: Platform Expansion of CUE-100 Series

CUE-100 Series T cell Engagers:
Targeting Selected Tumor Ags

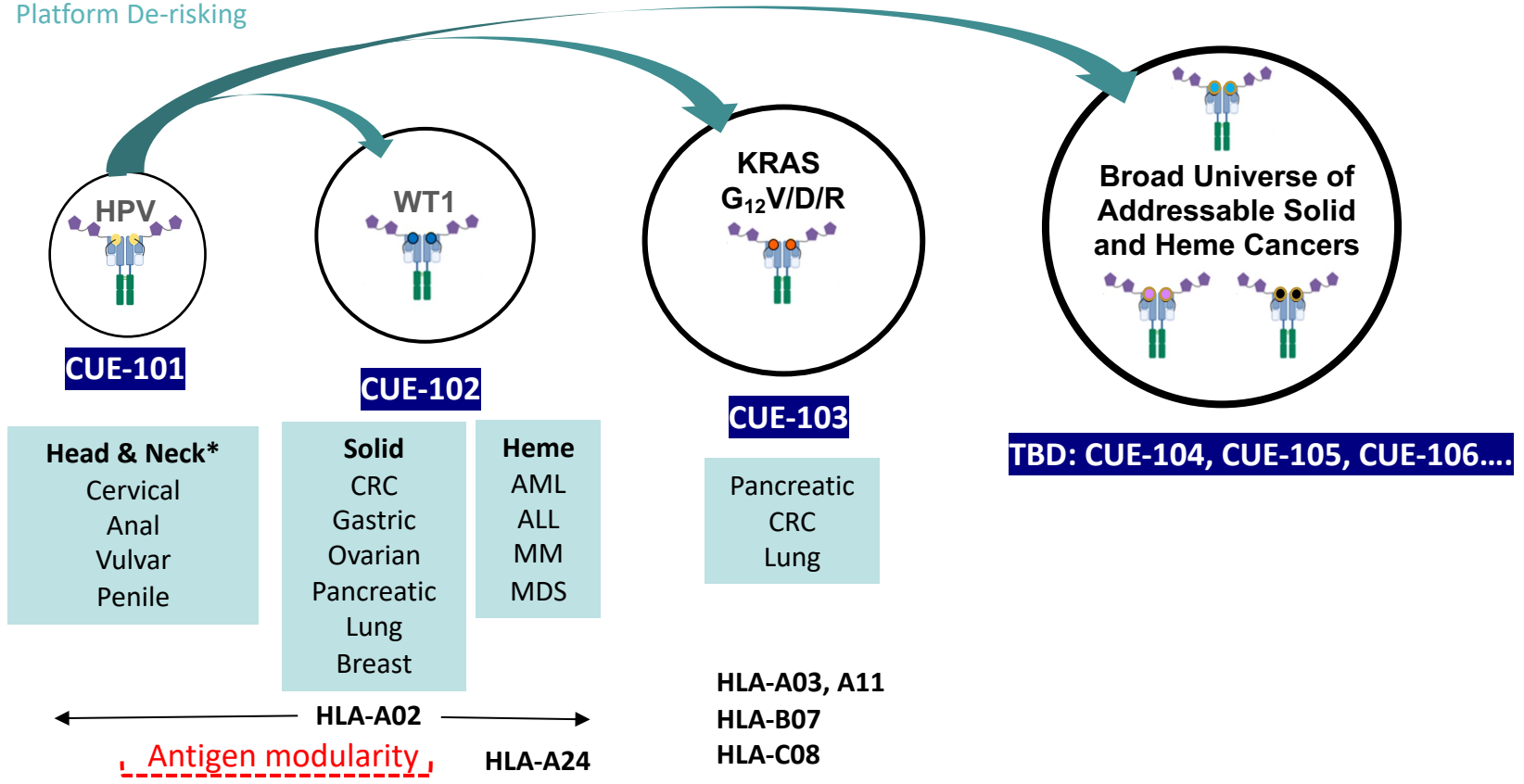


- Focus on validated, dominant tumor antigens
- ***Clinical PoC and platform de-risking via CUE-101***
- Structural similarity affords potential regulatory and development advantages

Clinical PoC with CUE-101 Provides a Springboard for Platform Expansion

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

⇨ Rapid Expansion into Broad Indications with Significant Unmet Need



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Key Milestones and Cash Position

- Define Potential Registrational studies for CUE-101 mono and combo therapy
  - Monotherapy registration study potential based upon mOS (tbd in Q4’ 22/Q1’23)
  - Combination therapy dose expansion to be completed 4Q’ 22 / 1Q’ 23
  - Combination therapy registration study potential (tbd 2H’23)
- Initiation of CUE-102 monotherapy clinical trial in WT1+ cancers (colon, gastric, pancreatic and ovarian) with patient dosing beginning July ‘22
  - Combination study of CUE-102 + CPI commencing once dose escalation in mono completed
- Advance allele expansion of CUE-100 series with CUE-103 in KRAS-mutant cancers to Phase 1 clinical trial (e.g., HLA A*03 and HLA A*11)
- Current cash position provides operational runway to Q4’23

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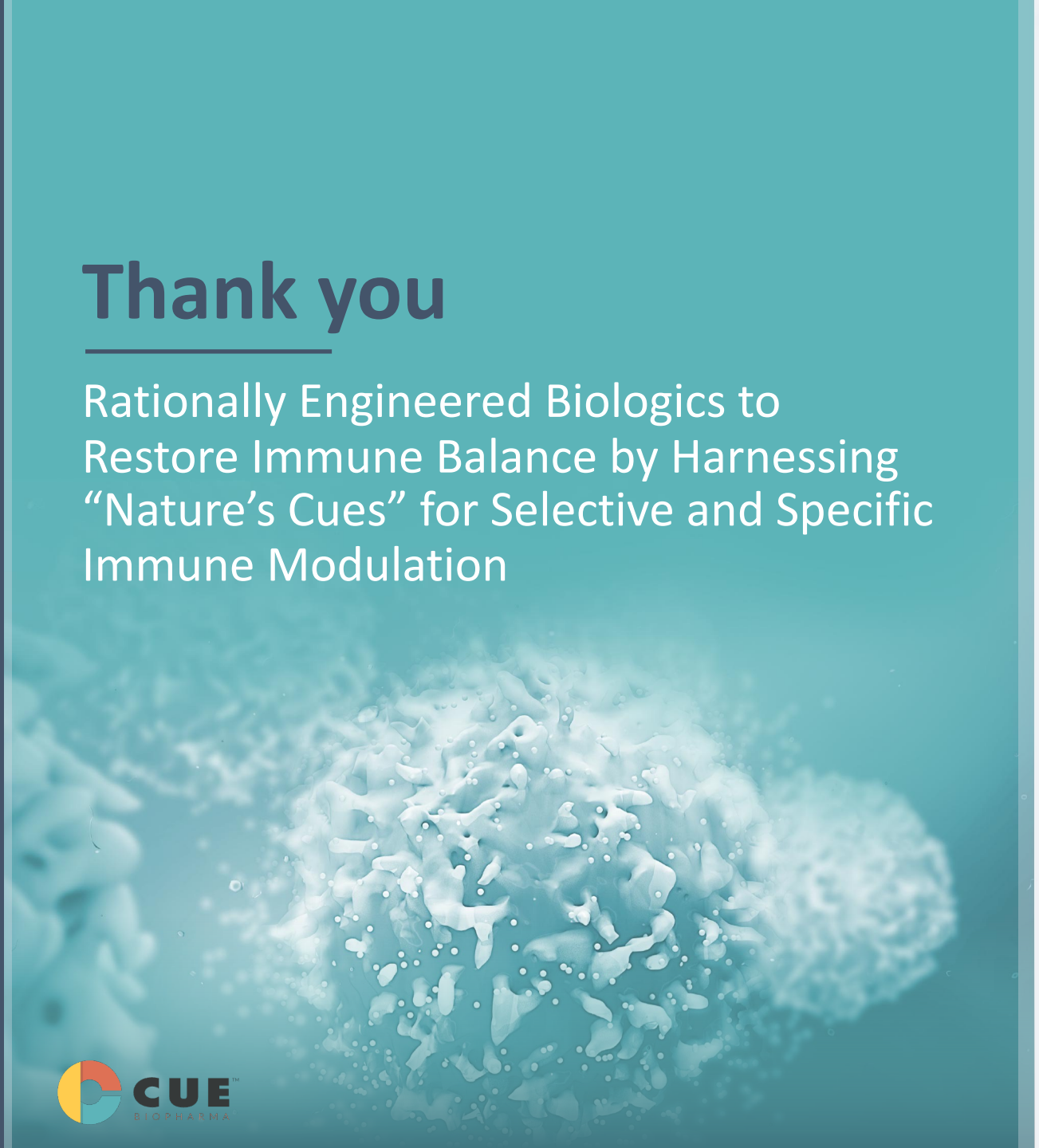
Thank you

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



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