

# Cue Biopharma, Inc.

Immune Responses, On Cue™

Nasdaq: CUE

March 2023



**CUE**™  
BIOPHARMA

# Forward-Looking Statements Disclosure

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# Well Positioned for Potential Breakthrough: Clinical Validation and Platform De-risking

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- Monotherapy efficacy in late-stage cancer patients – single-agent activity
- Significant increase to date in ORR in combination with CPI
- Favorable tolerability (>65 patients dosed, no VLS, CRS etc.)
- Ab-based design: favorable COGS (manufacturability) and stability (>36 mo.)
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# **Well Positioned for Potential Breakthrough: Capitalized into 2H'24 with current forecasted burn**

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- Fiscal discipline and program prioritization provides capital into 2H'24
- CUE-101 and CUE-102 address significant patient segments in solid cancers
- CUE-401 partnership with Ono Pharmaceuticals subsidizes development of promising autoimmune program with retained co-development right (US)
- Programs are well positioned (reduced risk due to CUE-101) for partnering with retained upside for shareholder value creation and risk mitigation In addition, partnering would extend cash runway

# Vision

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Translating “Nature’s Cues”  
into protein therapeutics

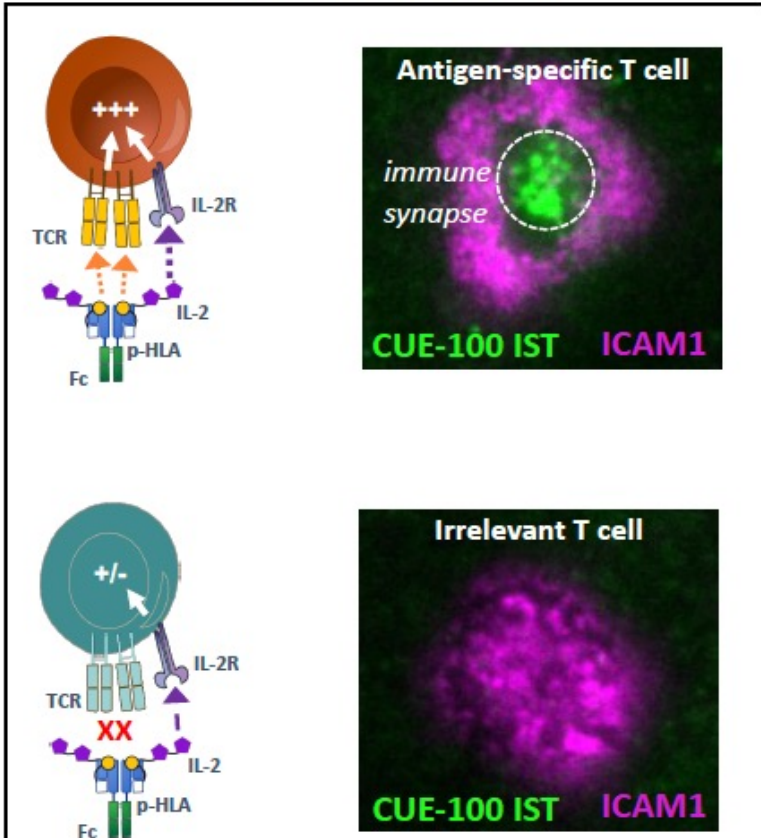
## Approach

- Generate a new class of bispecific T-cell engagers, termed Immuno-STATs™, for selective modulation of disease specific T cells
  - Approach in oncology: TCR-selective targeting of co-stimulatory signals, or activation signals, e.g., IL-2, to tumor specific T cells
- Clinically validate Immuno-STATs
  - Significant improvement in efficacy over current standard of care cancer immunotherapies
- Leverage and maximize platform modularity
  - Address unmet patient needs across a broad range of diseases



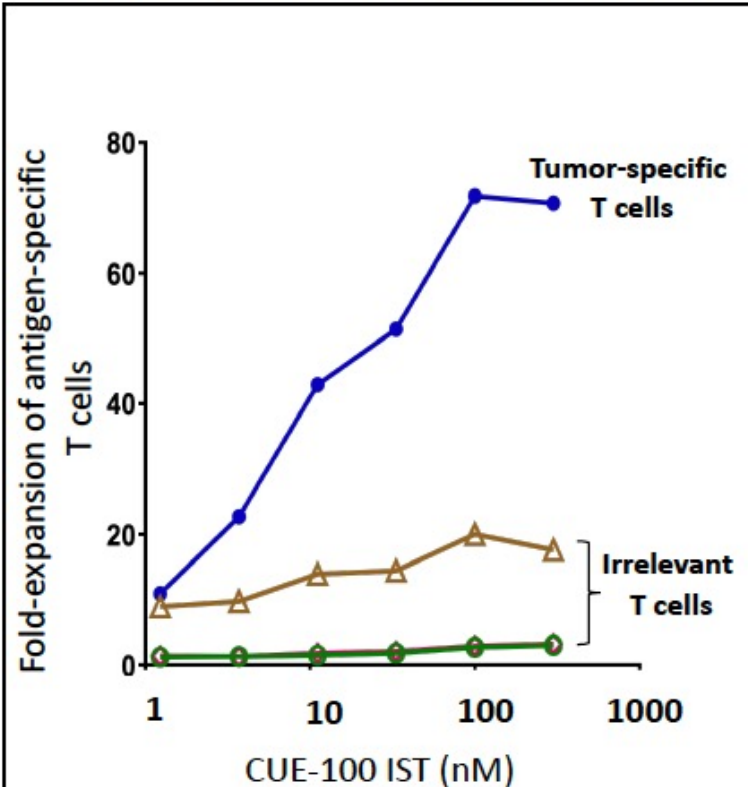
# CUE-100 Series ISTs: Tumor-specific T cell Engagers Enabling a Therapeutic Index for IL-2

## Selective Engagement (Immune Synapse)

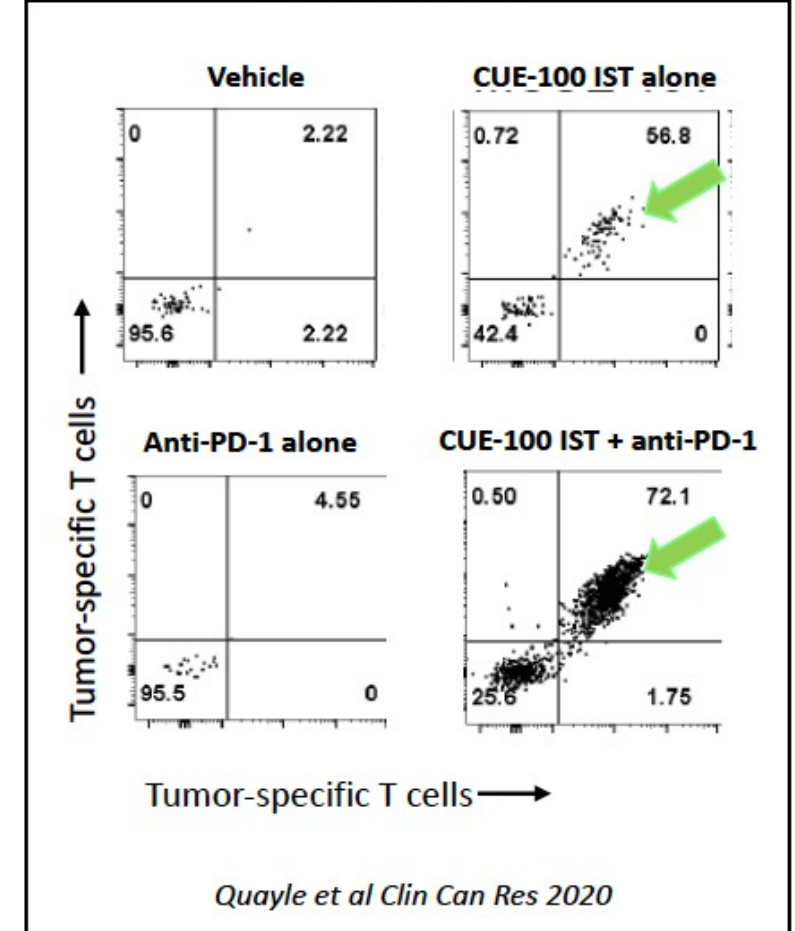


Collaboration with Dr. Michael Dustin, Univ. of Oxford

## Selective Expansion (Tumor-specific T cells from hPBMCs)



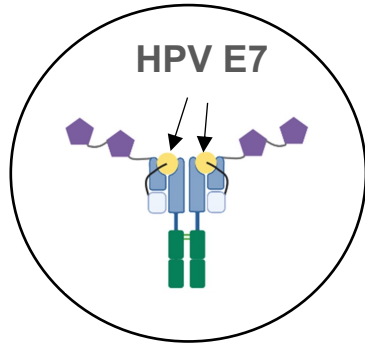
## T cell Activation in Tumors ("hot tumors")



The background features a teal color palette with abstract, organic shapes resembling splashes or liquid droplets. A horizontal white band runs across the middle of the image, serving as a backdrop for the title text. The overall aesthetic is clean and modern, with a focus on fluid, dynamic forms.

# **Clinical Validation and Platform De-risking**

# CUE-101 Provides Clinical PoC and Platform De-risking



**CUE-101**

**Head & Neck\***

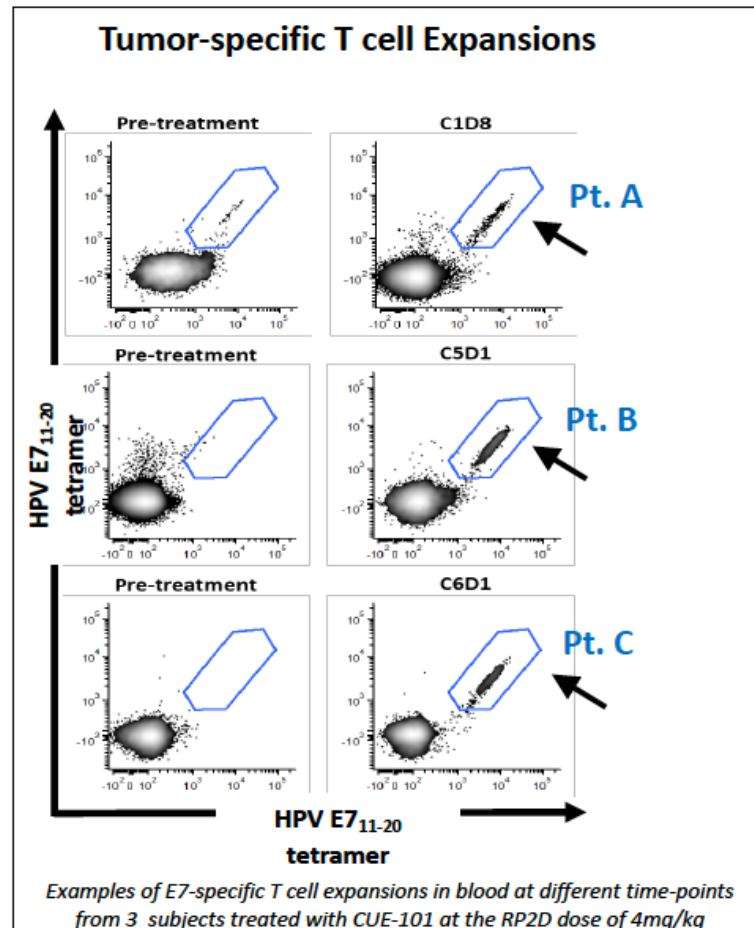
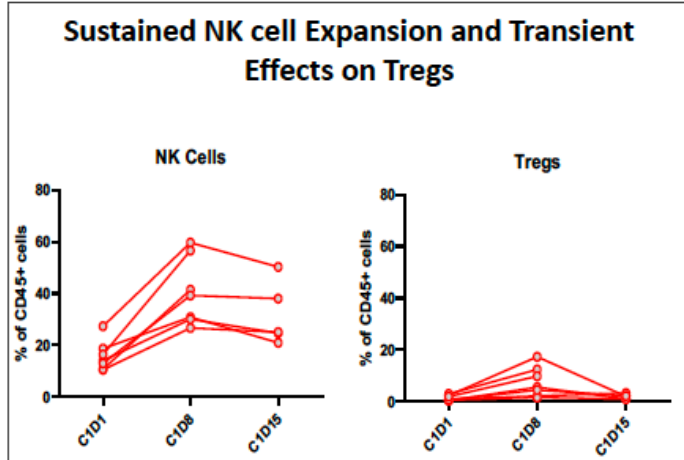
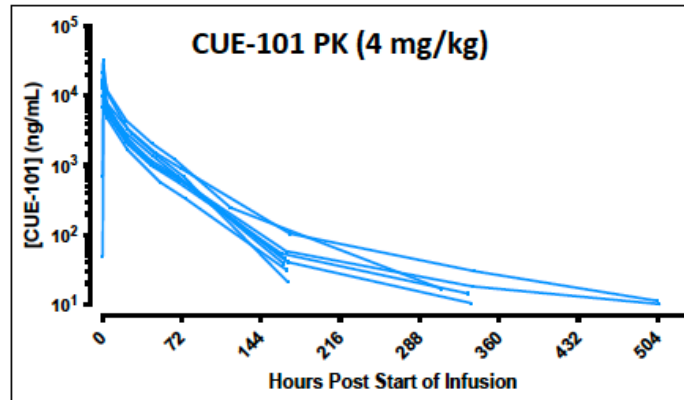
Anal  
Cervical  
Penile  
Vulvar

*\* Ongoing clinical trial*

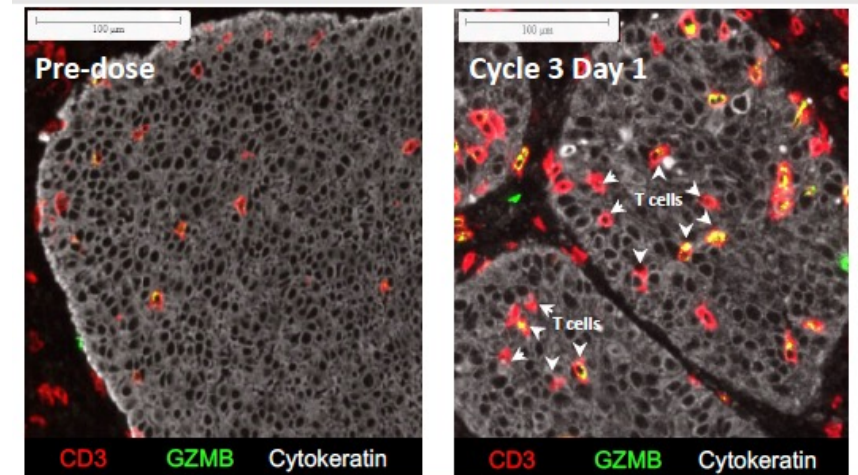
- CUE-101 Monotherapy in 3L+ R/M HNSCC
- CUE-101 + Pembrolizumab Combination in 1L R/M HNSCC
- CUE-101 Neo-adjuvant Trial in locally/advanced HNSCC
  - Trial ongoing at Washington University in St. Louis



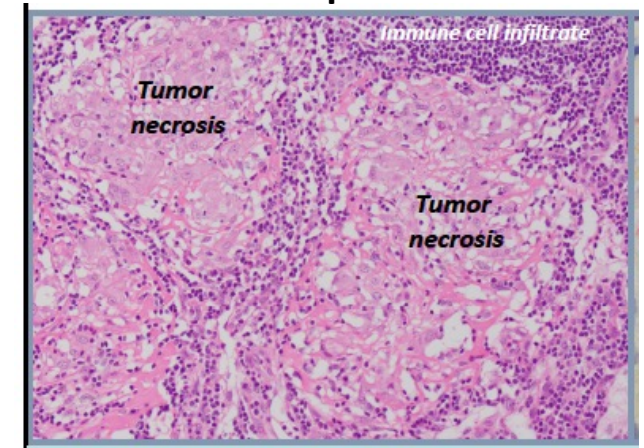
# CUE-101 Monotherapy Patient Data: PK, PD and Tumor Infiltration



## T cell infiltration into tumors post-CUE-101 Tx

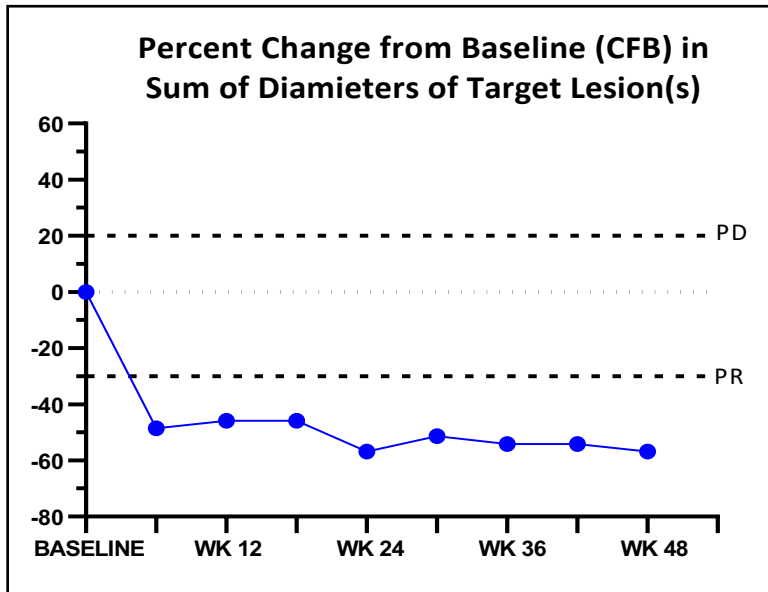


## Tumor necrosis post-CUE-101 Tx



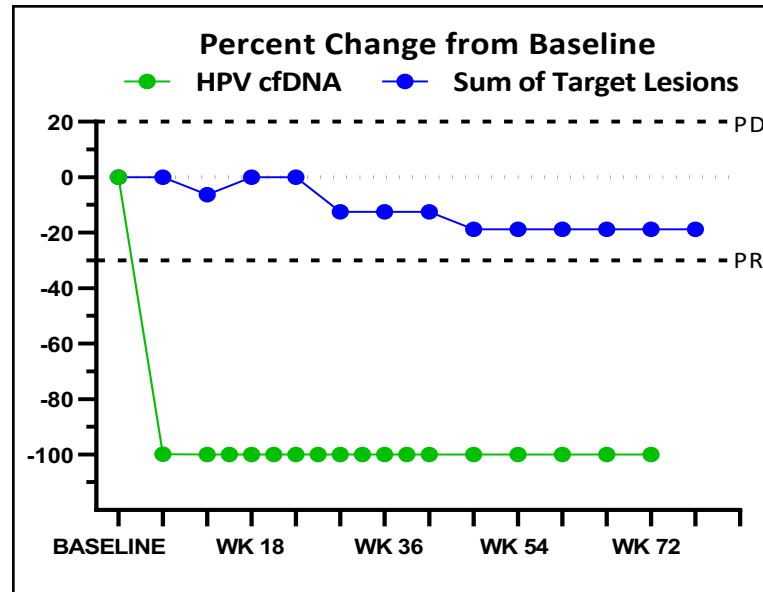
# CUE-101 Monotherapy: Patterns of Clinical Efficacy in 3L+ R/M HNSCC Patients

Patient A



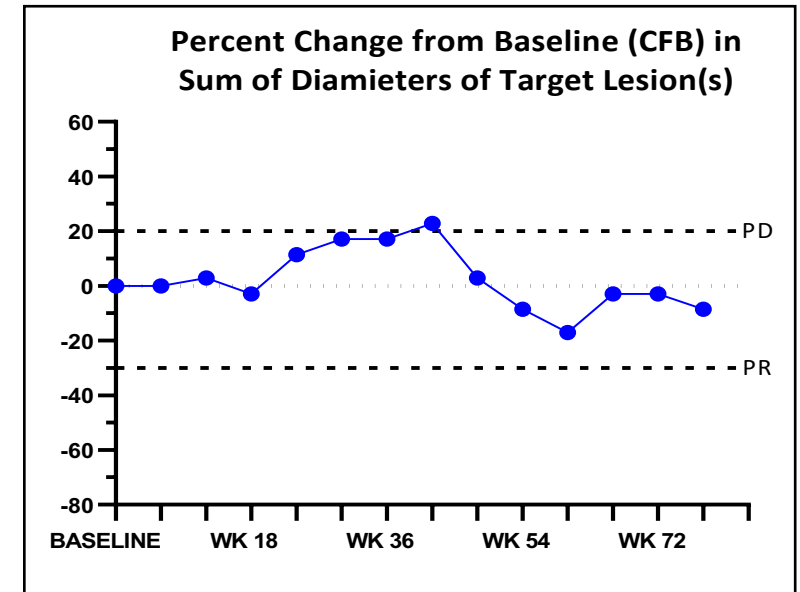
- Rapid tumor reduction and durable PR
- Remained on treatment for ~1 year

Patient B



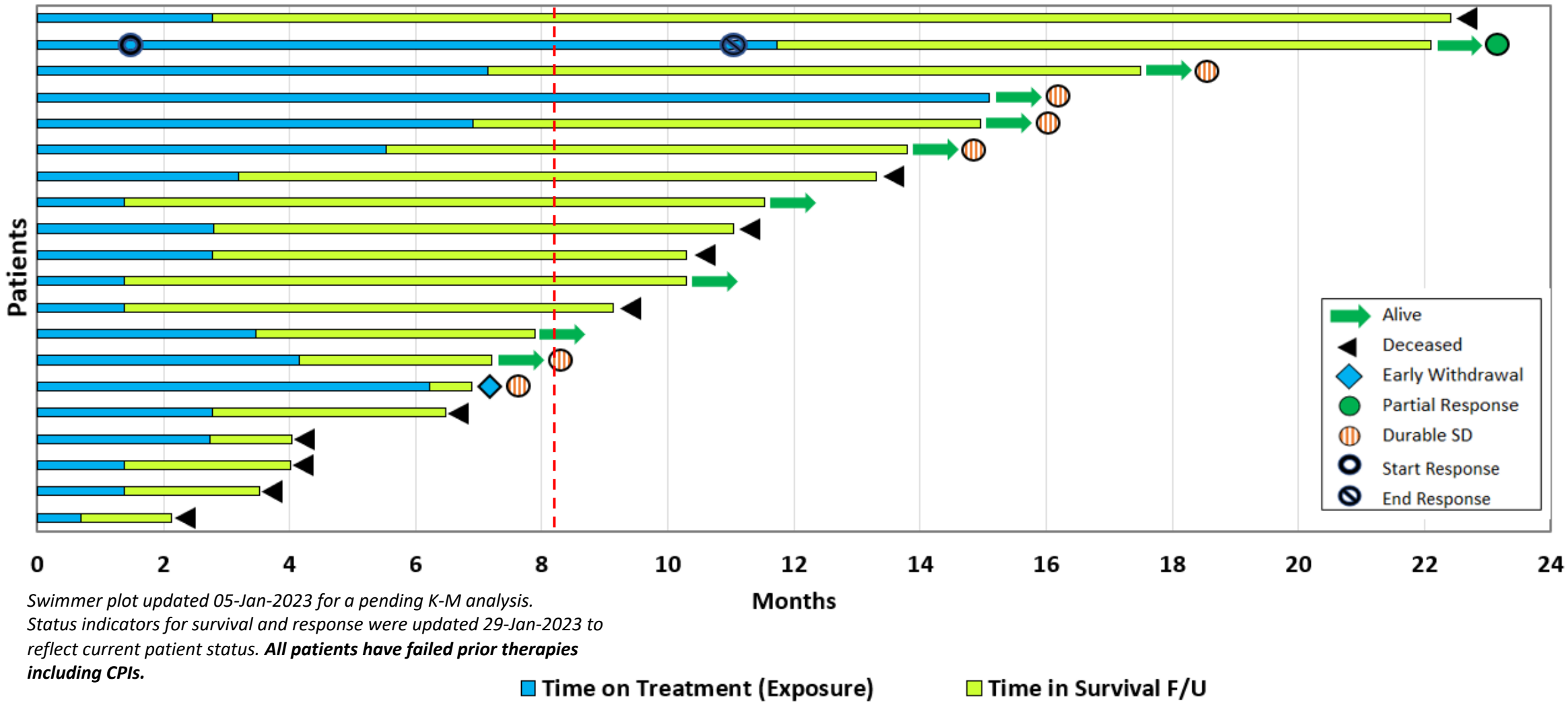
- Durable SD with sustained non-detectable levels of HPV cfDNA
- Remains on treatment for >18 months

Patient C



- Durable SD
- Remained on treatment for >18 months

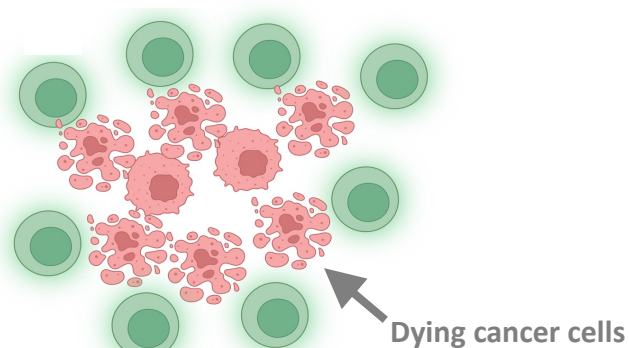
# Overall Survival in Monotherapy 4 mg/kg Patients



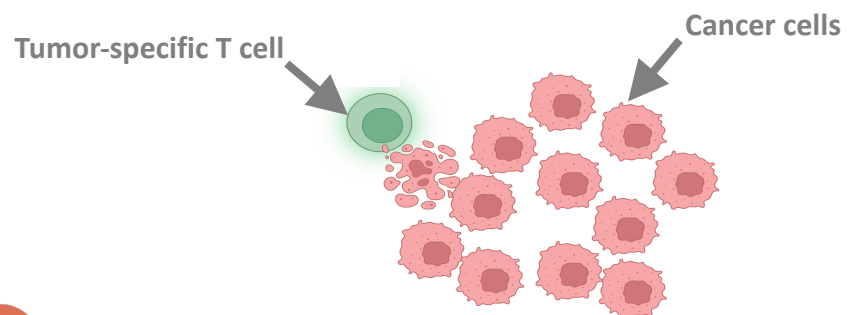
# Complementary Mechanisms with CUE-101 + Checkpoint Inhibition

## Complementary MoA with CUE-101 and anti-PD-1

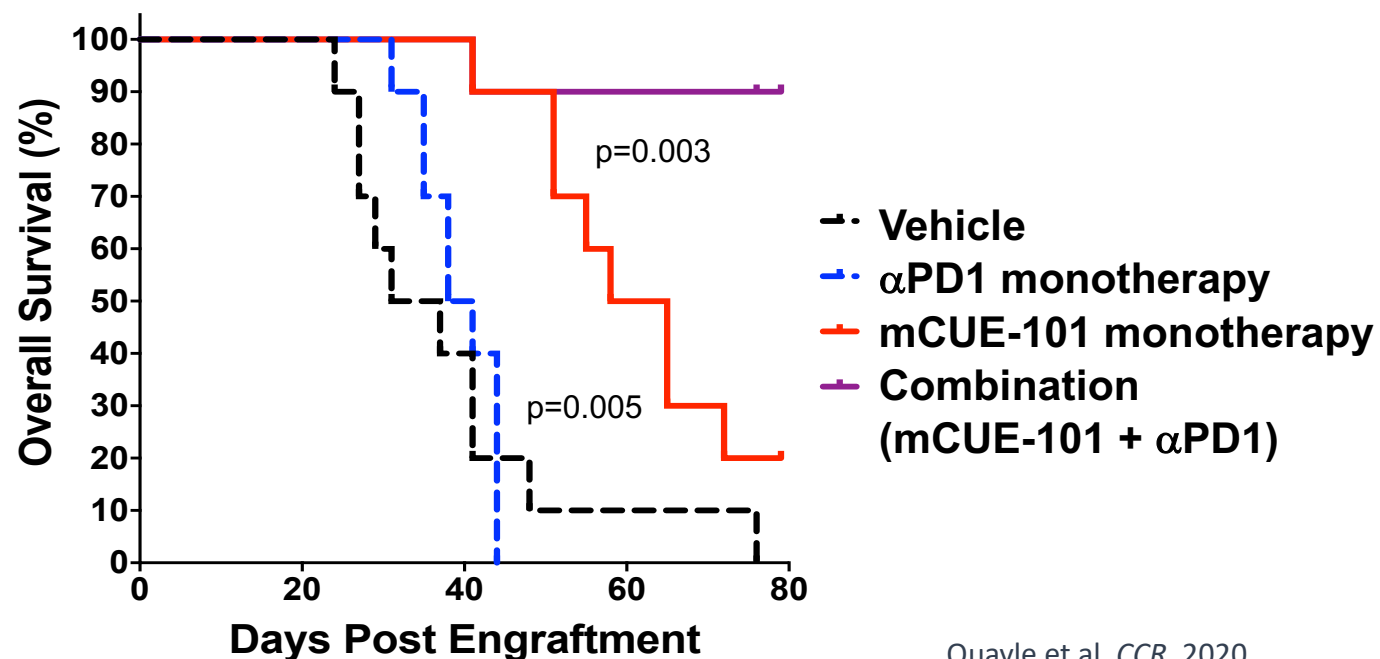
### CUE-101 + Anti-PD-1 treatment



### Anti-PD-1 treatment alone

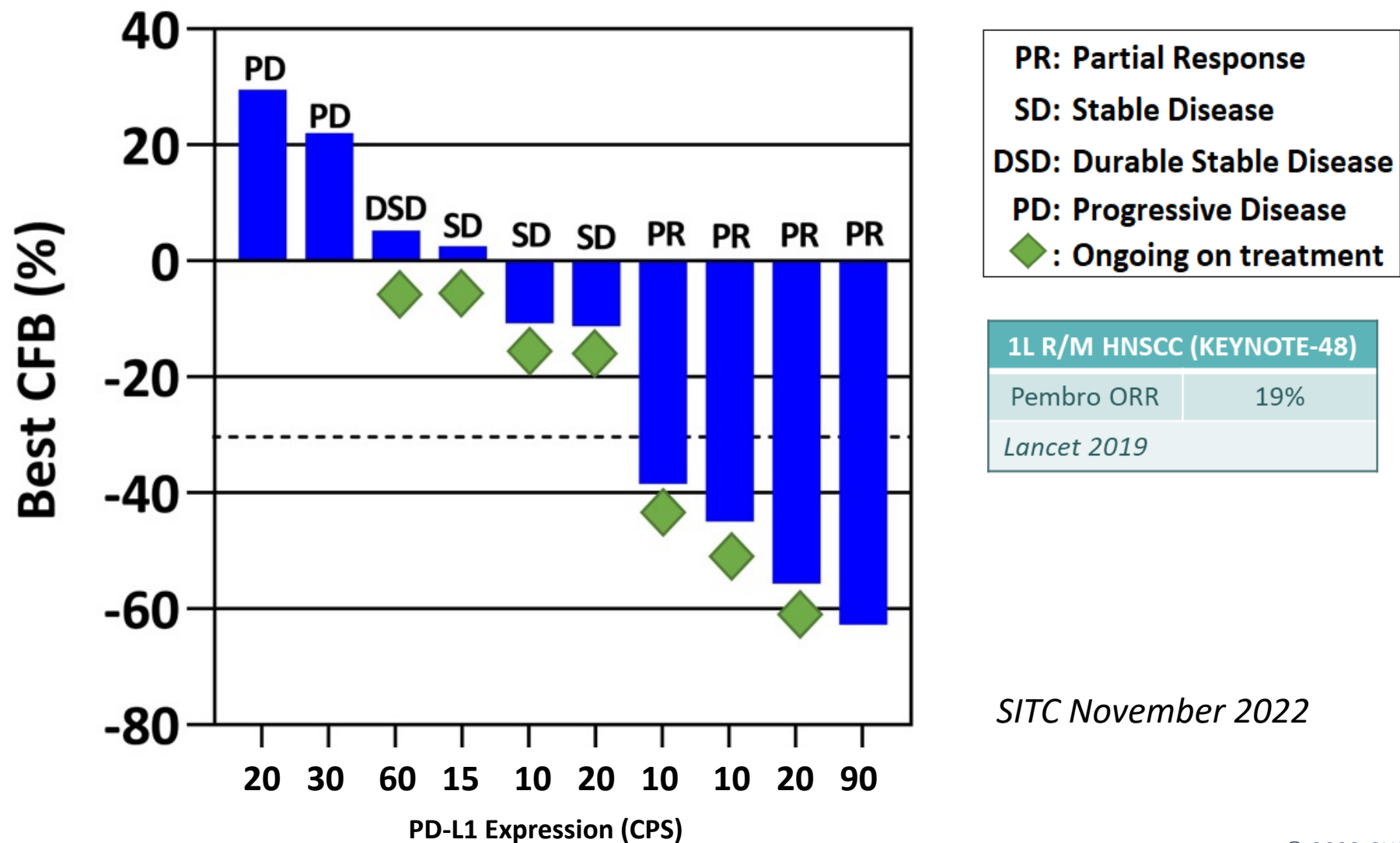


## Preclinical studies demonstrated enhanced response and survival following CUE-101 + anti-PD-1 combo therapy



Quayle et al, CCR, 2020

# CUE-101 in Combination with Pembrolizumab in 1L R/M HNSCC: 40% ORR at 4 mg/kg RP2D (*vs. 19% historical ORR with pembro alone*)





# CUE-101: Clinical Validation and Platform De-risking

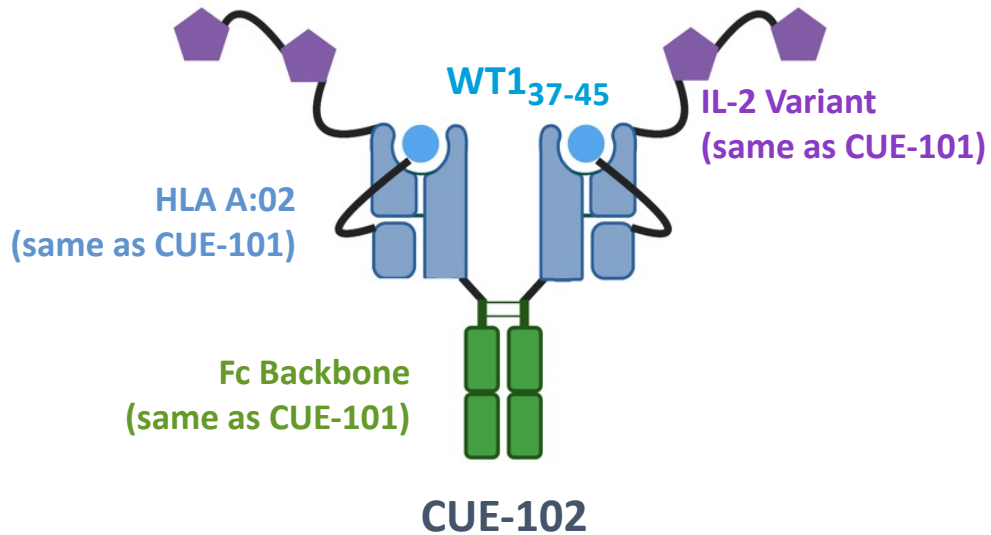
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- ✓ **Tolerability at Efficacious doses**
- ✓ **Demonstration of single-agent anti-tumor efficacy**
  - *RECIST-based PR and DSD in 3L+ R/M HNSCC patients*
  - *mOS benefit emerging from survival follow-up*
- ✓ **Significant enhancement of clinical efficacy in combination with CPI in 1L R/M HNSCC**
  - *40% ORR in combo w/ pembro vs ~19% ORR pembro alone as reported at SITC November 2022*
  - *PFS and mOS maturing*
  - *Plan to present updated data with additional patients at upcoming oncology conference*
- ✓ **Fast Track Designation granted for both monotherapy and combination therapy (Oct. 2022)**

# CUE-102 Wilms Tumor 1 (WT1): Broad Potential Opportunity in Multiple Solid and Heme Cancers

## Molecular Design

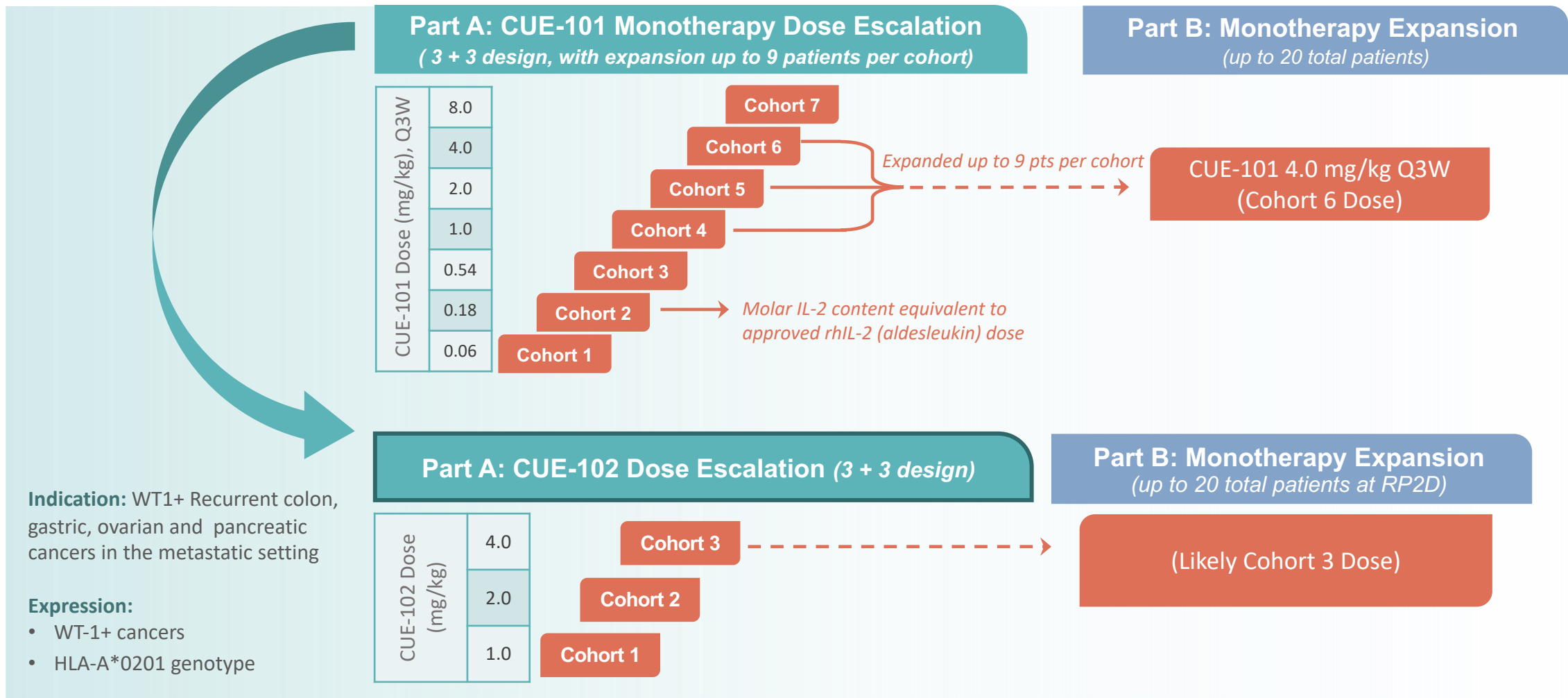
(99% sequence identity to CUE-101)



- IND approval for CUE-102 harnessed the clinical de-risking observed with CUE-101, leading to potential advantages:
  - Clinical development efficiencies (approval to start at a higher dose and minimize cohorts for dose escalation)
  - Regulatory advantages (FDA did not require additional IND tox)
- CUE-102 targets a dominant T cell epitope from WT1
- WT1 is an attractive onco-fetal tumor antigen with significant expression in numerous solid and heme cancers
  - Solid: CRC, Ovarian, Lung, Gastric, Pancreatic, Breast, GBM
  - Heme: AML/MDS, ALL, MM

**Phase 1 Monotherapy Trial Currently Enrolling (NCT05360680)**

# CUE-101 Accelerates CUE-102 Clinical Development by Enabling Dose Escalation to Start at 1 mg/ kg



**Abbreviations:** Q3W, once every 3 weeks; rhIL-2, recombinant human interleukin-2; RP2D, Recommended Phase 2 Dose

# Executive Summary: Immuno-STAT (IST) Platform

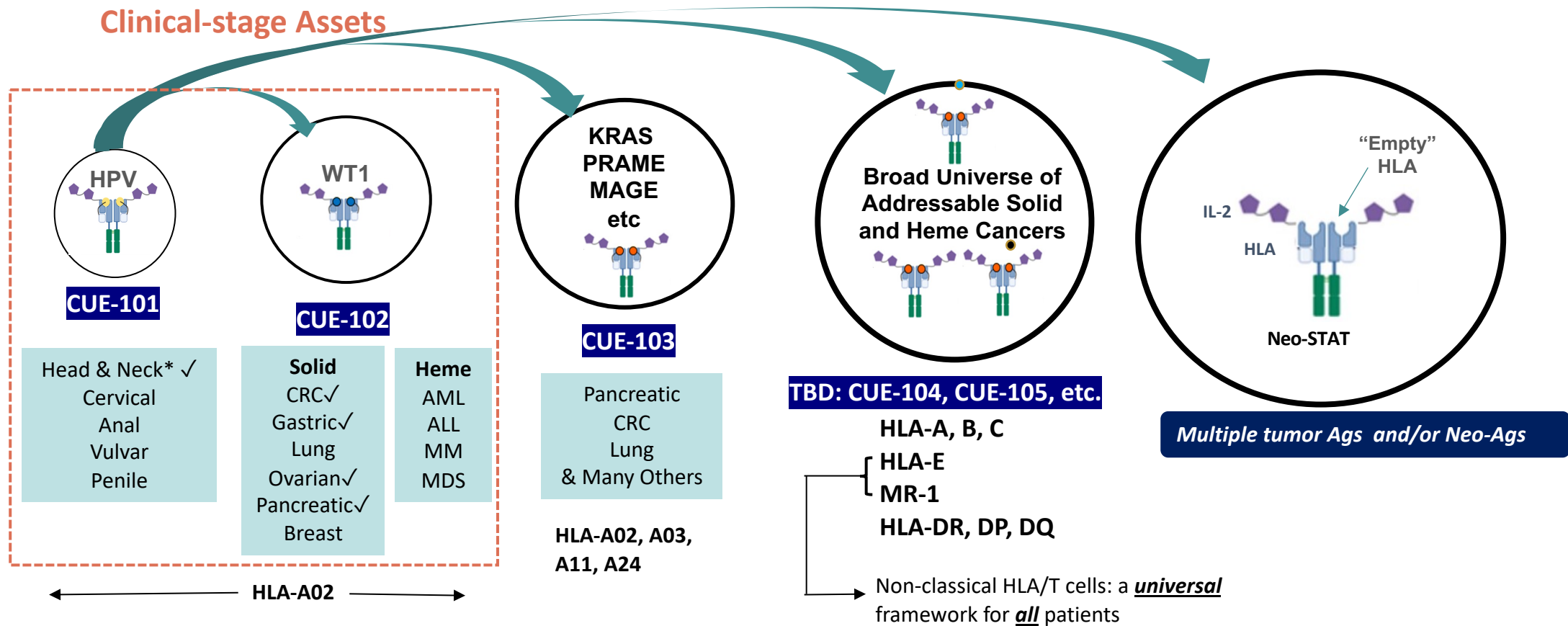
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- CUE-100 series generates a **therapeutic index for IL-2** by selective targeting of anti-tumor T cells, which presents a broad opportunity for addressing many cancers
  - *Strategy for creating a therapeutic index can be deployed for any other cytokine or immune activation signal*
- CUE-101, the lead clinical candidate supports platform de-risking and clinical validation of CUE-100
- CUE-101 clinical efficacy data supports potential for multiple registrational paths in distinct lines of therapy with significant commercial potential
- Platform expansion via additional pipeline assets offers potential for targeting multiple indications
  - *CUE-102 in ovarian, CRC, gastric and pancreatic (trial ongoing); additional opportunities in lung, breast, AML, MM*
  - *Additional pipeline assets targeting mutated KRAS, MAGE-A4, PRAME etc.*

# BROAD Opportunities for CUE-100 Series in Cancer Immunotherapy

*Clinical PoC with CUE-101 Provides a Springboard for Platform Expansion into Broad Indications*

## Clinical-stage Assets



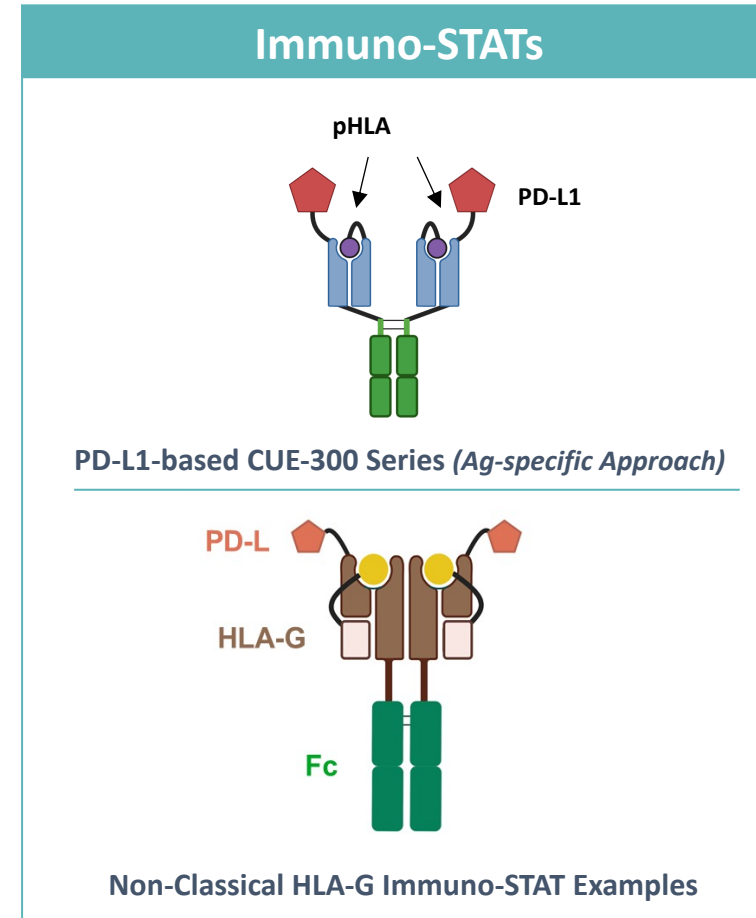
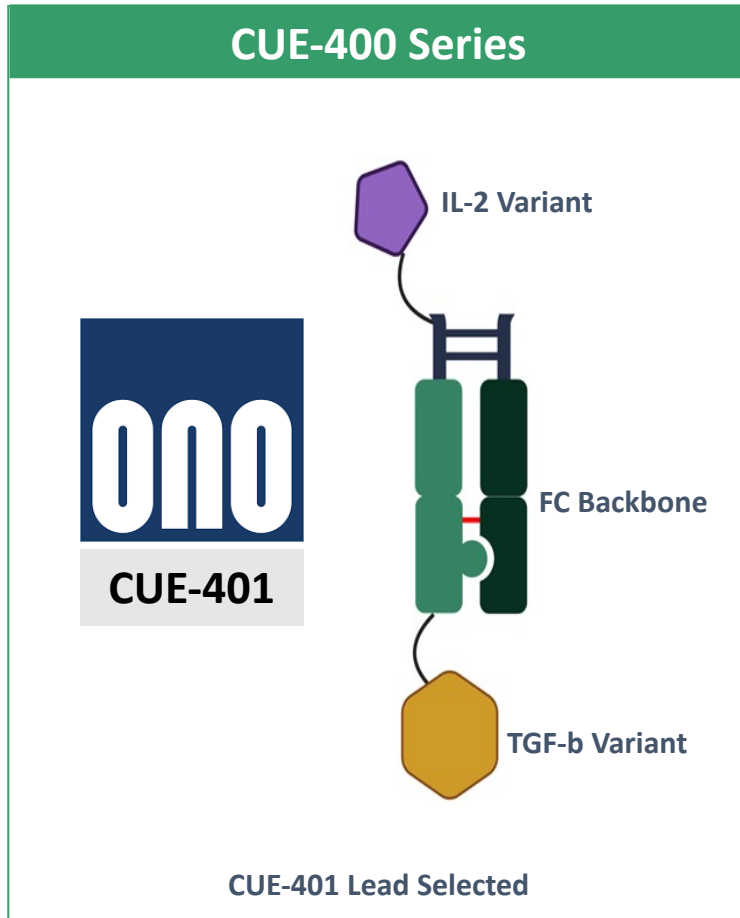
*Structural similarity creates potential regulatory and development efficiencies*





**Autoimmune**

# CUE-AI: Pipeline of Novel Biologics for Resetting Tolerance



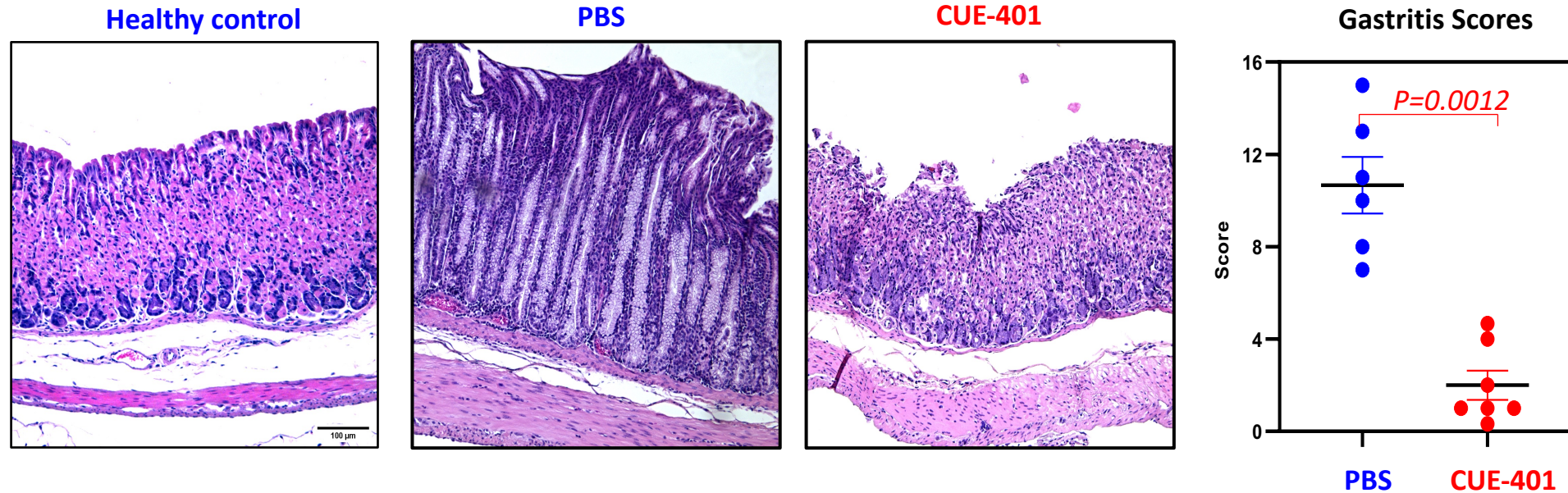
*Initial Feasibility with Broad IP Coverage  
Biological Evaluation Gated by Resourcing*

# CUE-401 Overview

- **Highly Differentiated Opportunity to Reset Immune Balance**
  - CUE-401 induces new Tregs and expands pre-existing nTregs
  - CUE-401's MoA demonstrates in vivo conversion of autoreactive T cells into Tregs, which is a fundamental mechanism for re-setting immune balance
  - Vast therapeutic potential across many T cell mediated autoimmune and inflammatory diseases
- **Significant Superior Differentiation** over all other CD25-specific IL-2 muteins that selectively focus only on the small fraction of nTregs

	<u>IL-2 Muteins</u>	<u>CUE-401</u>
↑ nTregs	✓ Yes	✓ Yes
↑ iTregs	✗ No	✓ Yes
Generate Ag-specific Tregs	✗ No	✓ Yes

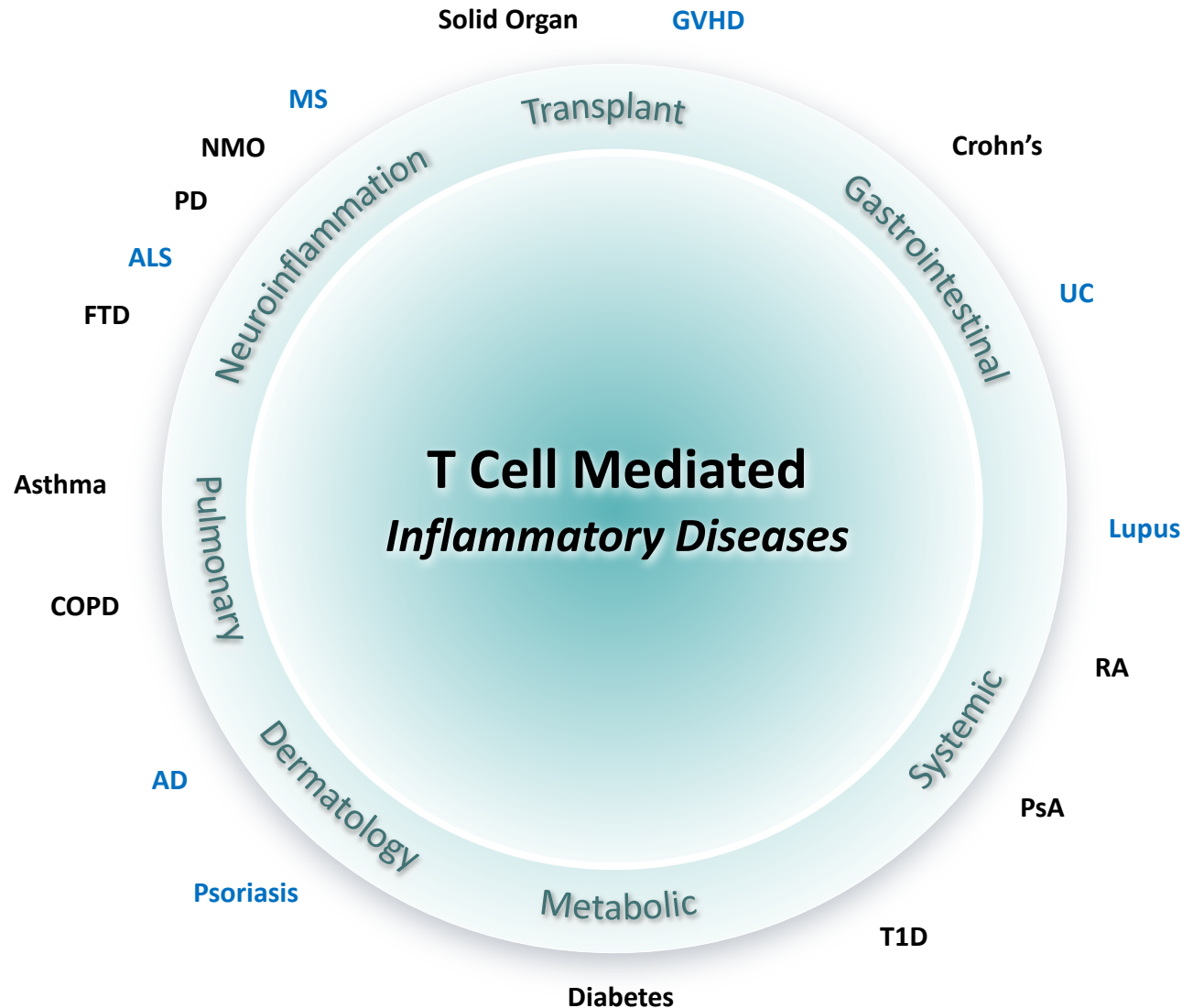
# CUE-401: Short-term Treatment Results in Long-term Protection from Autoimmune Gastritis



*Collaboration w/ Dr. Rich DiPaolo, SLU*

- CUE-401 treatment results in significant protection from tissue destruction
- Initial short-term treatment (d1, d14) with CUE-401 results in long-term protection (d60+, as shown above)

# CUE-401: Potential to Address Unmet Patient Needs Across a Broad Range of T Cell Mediated Inflammatory Diseases



**Bold** = Active industry trials with IL-2 muteins and tolerance approaches



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# Platform Developments for Sustained Value Creation

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## Oncology

- Emerging as solution provider of selective cancer-specific T cell activation: exemplified by CUE-101
  - CUE-101 clinical data will drive near-term value (monotherapy/combination with CPI)
  - CUE-102 clinical data will further validate platform and modularity – represents potential value amplifier
- Modular/scalable platform for broad patient coverage (various cancers/various alleles)
  - Potential solution provider for personalized immunotherapy via Neo-STAT™

## Autoimmune

CUE-400, as well as CUE-300 represent potential transformative breakthroughs in AI disease with broad market potential

- Ono Pharmaceuticals strategic partnership provides financial support with Cue Biopharma retaining co-development
- Option with 50% of US market, milestones (subsidizing significant portion of Cue Biopharma's co-development costs)

# Thank You

## Immune Responses, On Cue™

*Harnessing the Potential of the Human  
Immune System to Treat Cancer*



**CUE**™  
BIOPHARMA