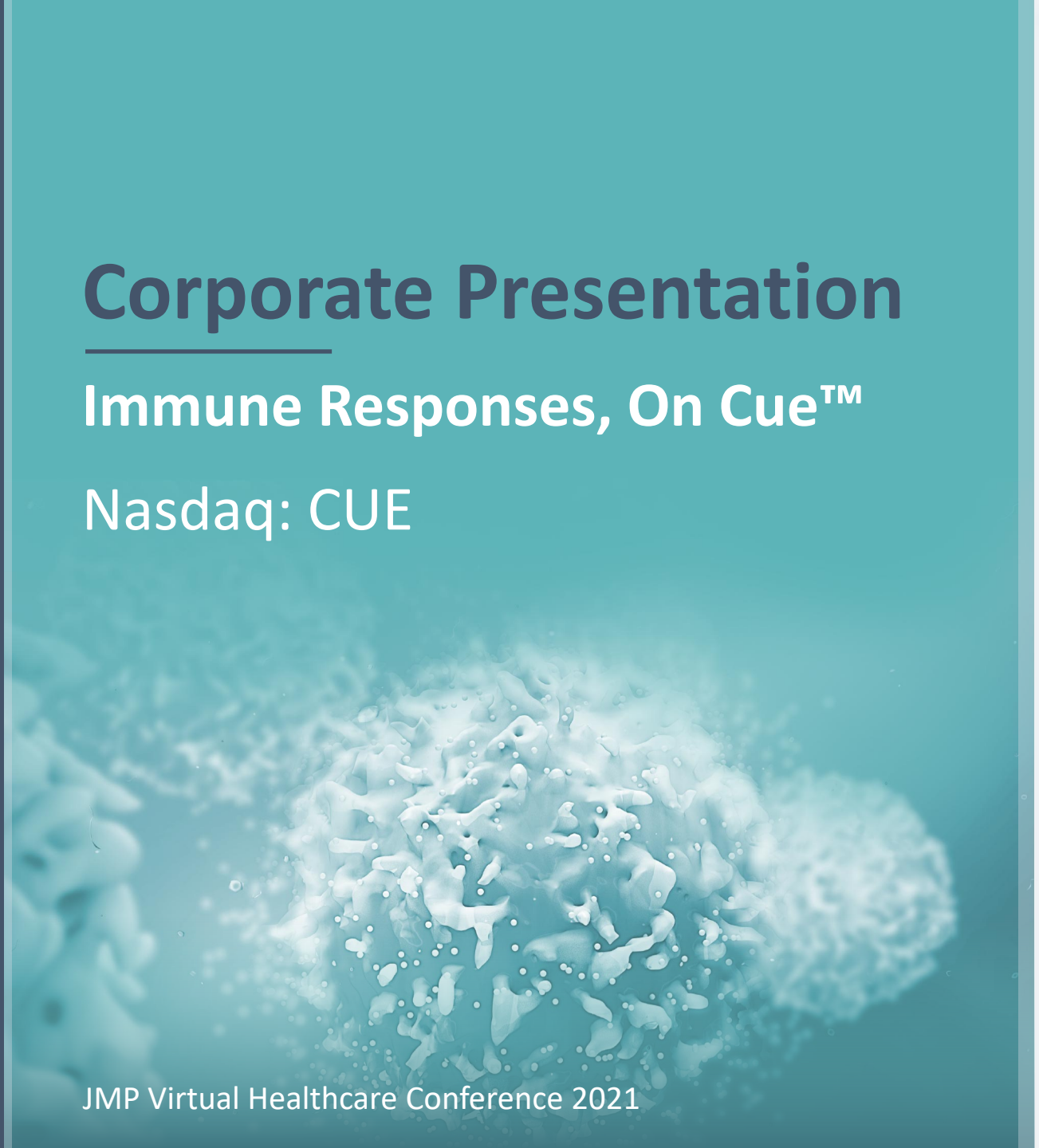
Corporate Presentation

Immune Responses, On Cue™

Nasdaq: CUE



JMP Virtual Healthcare Conference 2021

CUE™
BIOPHARMA

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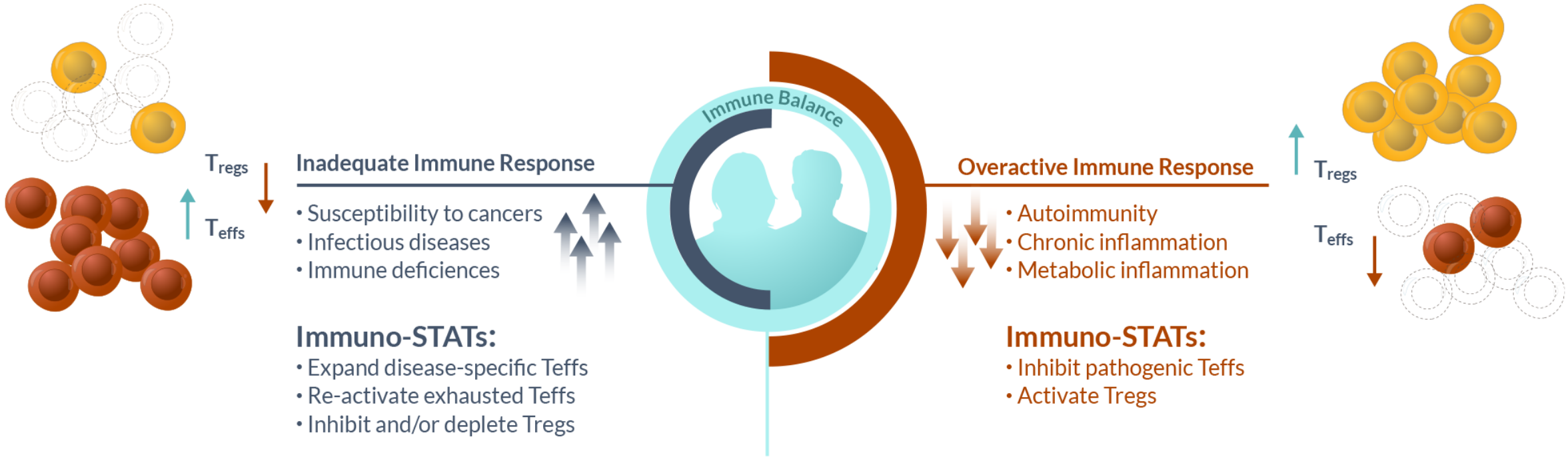
Rationally Engineered Biologics to Restore Immune Balance by Harnessing Nature's "Cues" for Selective and Specific Immune Modulation

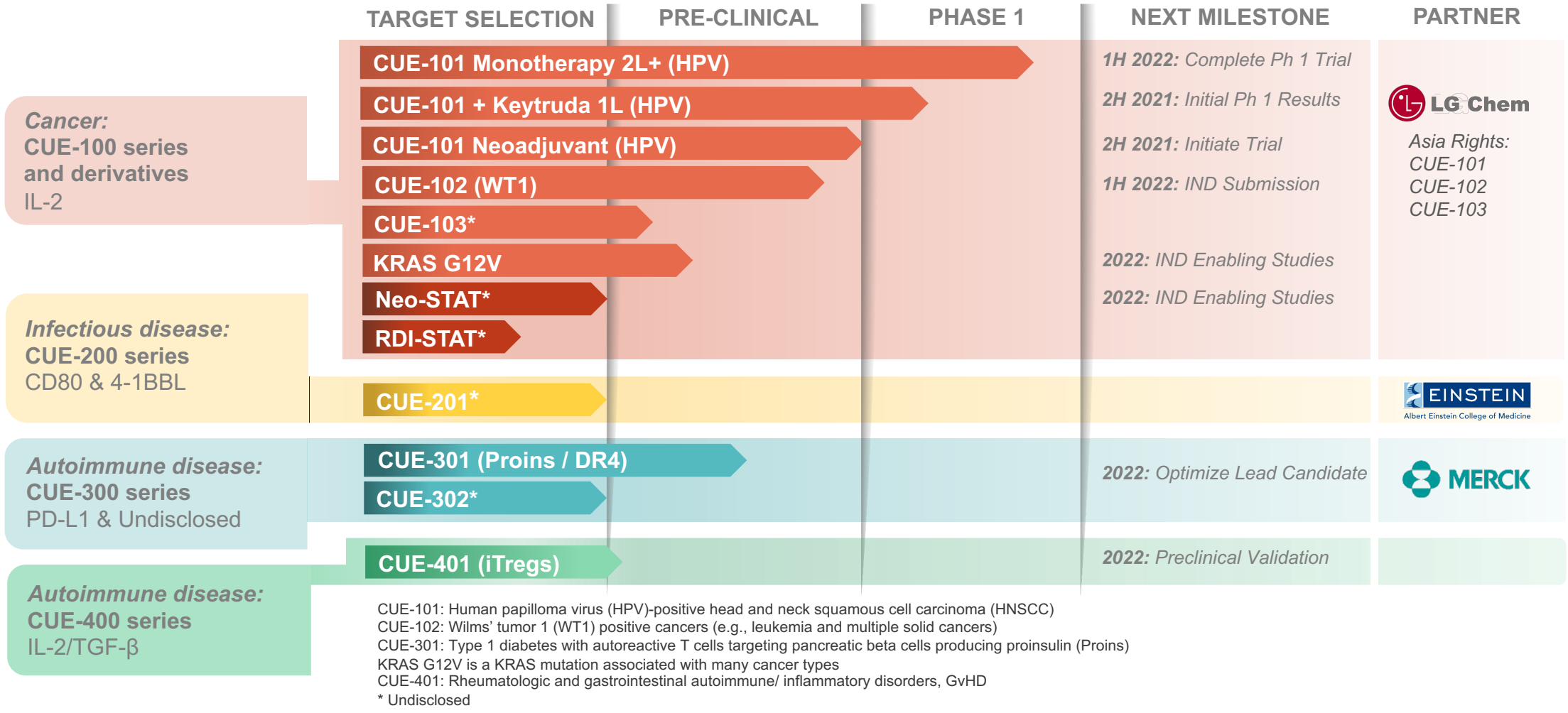
Restoring Immune Balance



Restoration of immune balance is a key pillar of human health

KEY: T_{effs}, effector T cells; T_{regs}, regulatory T cells

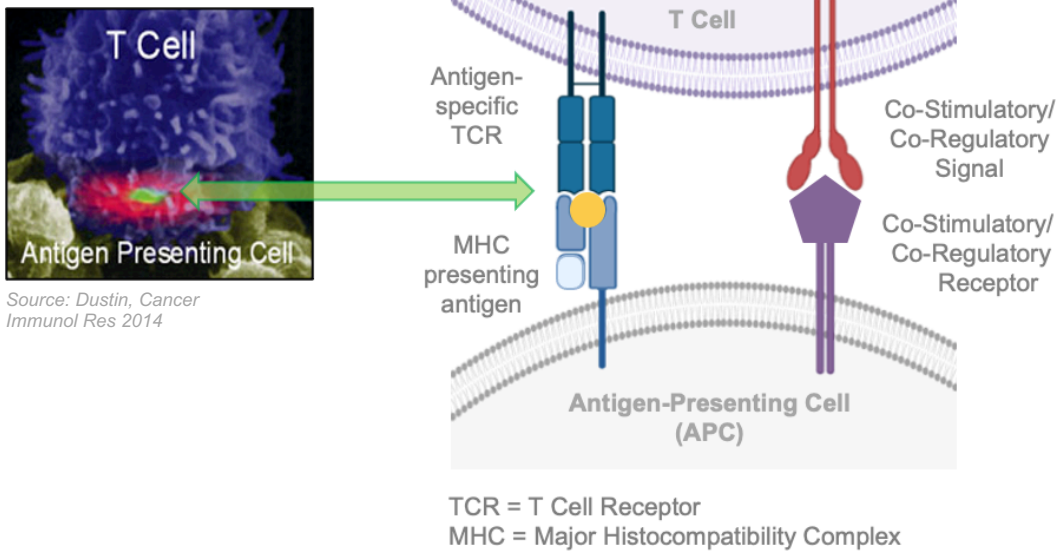
Cue Biopharma Drug Product Candidate Pipeline

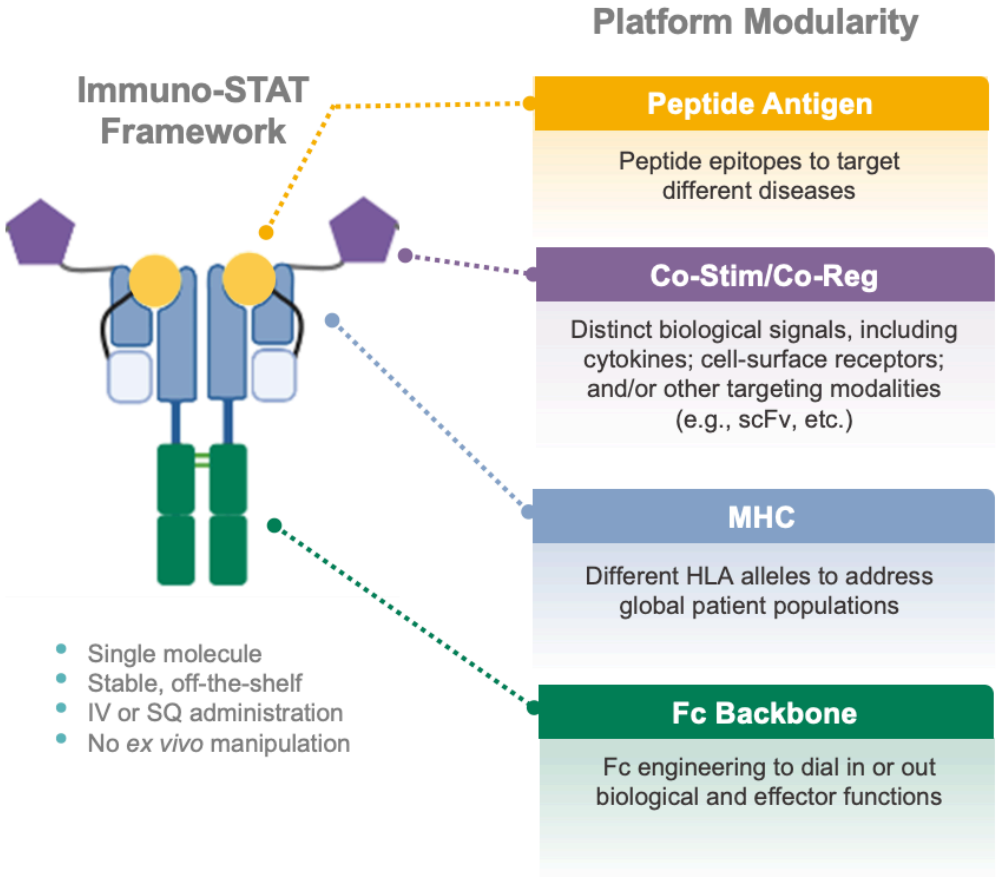


CUE-101: Human papilloma virus (HPV)-positive head and neck squamous cell carcinoma (HNSCC)
CUE-102: Wilms' tumor 1 (WT1) positive cancers (e.g., leukemia and multiple solid cancers)
CUE-301: Type 1 diabetes with autoreactive T cells targeting pancreatic beta cells producing proinsulin (Proins)
KRAS G12V is a KRAS mutation associated with many cancer types
CUE-401: Rheumatologic and gastrointestinal autoimmune/ inflammatory disorders, GvHD
* Undisclosed

Immuno-STAT: Emulating Nature's Cues to Selectively Modulate T Cells

The Immuno-STAT platform can generate a diversity of therapeutic molecules to selectively target and modulate the activity of a broad range of disease-relevant T cells





CUE 100 Series: Immuno-STAT Basic Structure

CUE-100 Series is designed for biased targeting of IL-2 to tumor-specific T cells

“Signal 1” T Cell Receptor (TCR) engagement of tumor-specific T cells

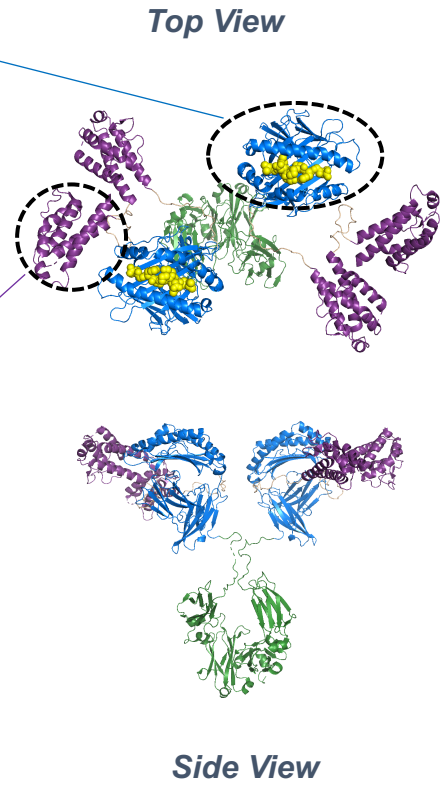
Tumor-Peptide Loaded HLA

“Signal 2” co-stimulatory ligand

- ***Abrogate binding to IL-2Rα: Minimize Treg activation and improves safety***
- ***Attenuate binding to IL-2Rβ: Allows for selective activation of tumor-specific T cells***

Engineered IL-2 Variant

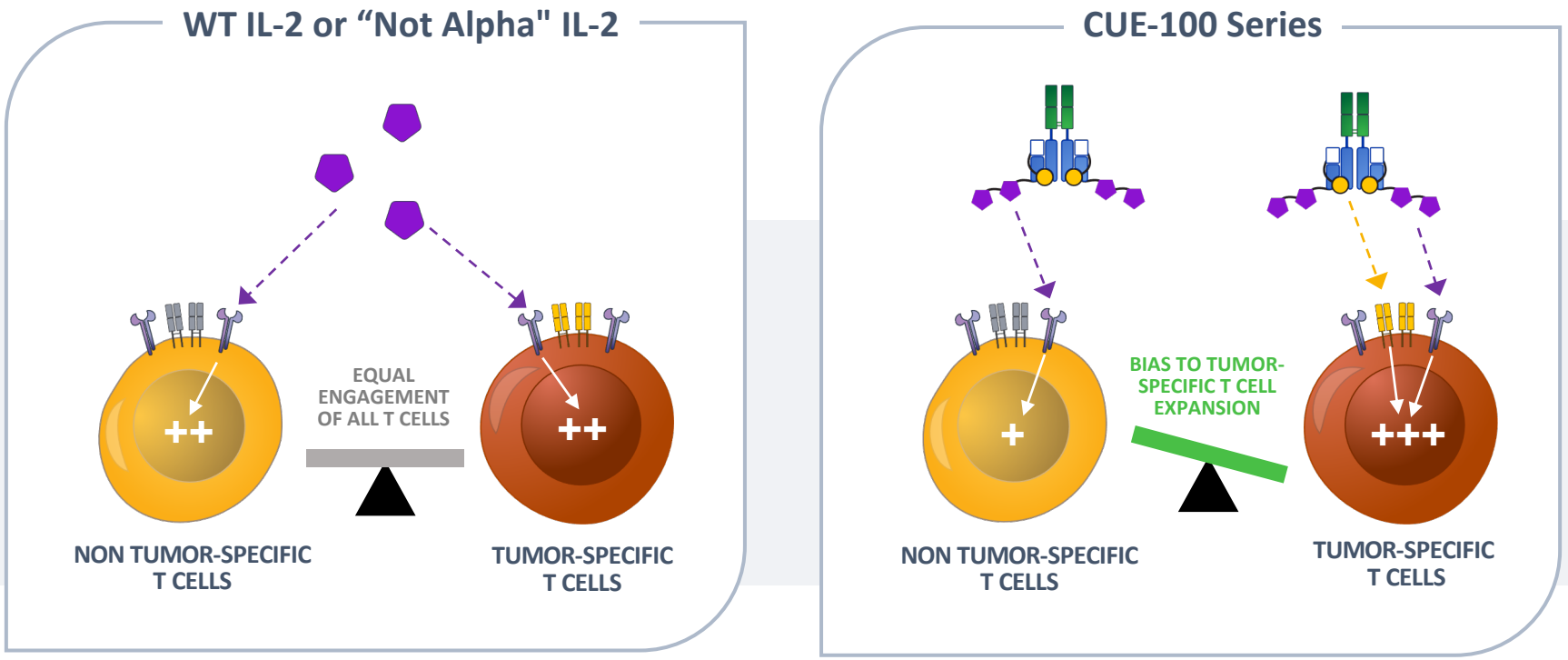
CUE-100 Series



CUE-100 Series: Harnessing IL-2 and TCR Signals for Improved Selectivity and Tolerability

IL-2 selectivity for tumor-specific T cells activation and enhanced tolerability

Proposed MoA

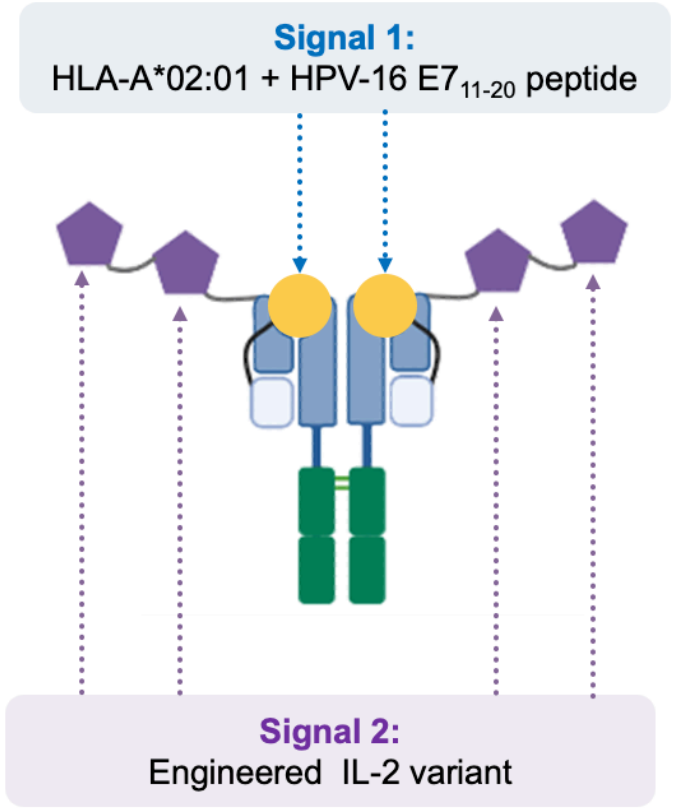


TOLERATED DOSE:

Aldesleukin:	0.037 mg/kg (approved dose)
NKTR-214:	0.006 mg/kg (RP2D)
ALKS-4230:	0.006 mg/kg (RP2D)
THOR-707:	0.006 to 0.024 mg/kg

CUE-101: 0.06 mg/kg to 8.0 mg/kg
NO MTD identified

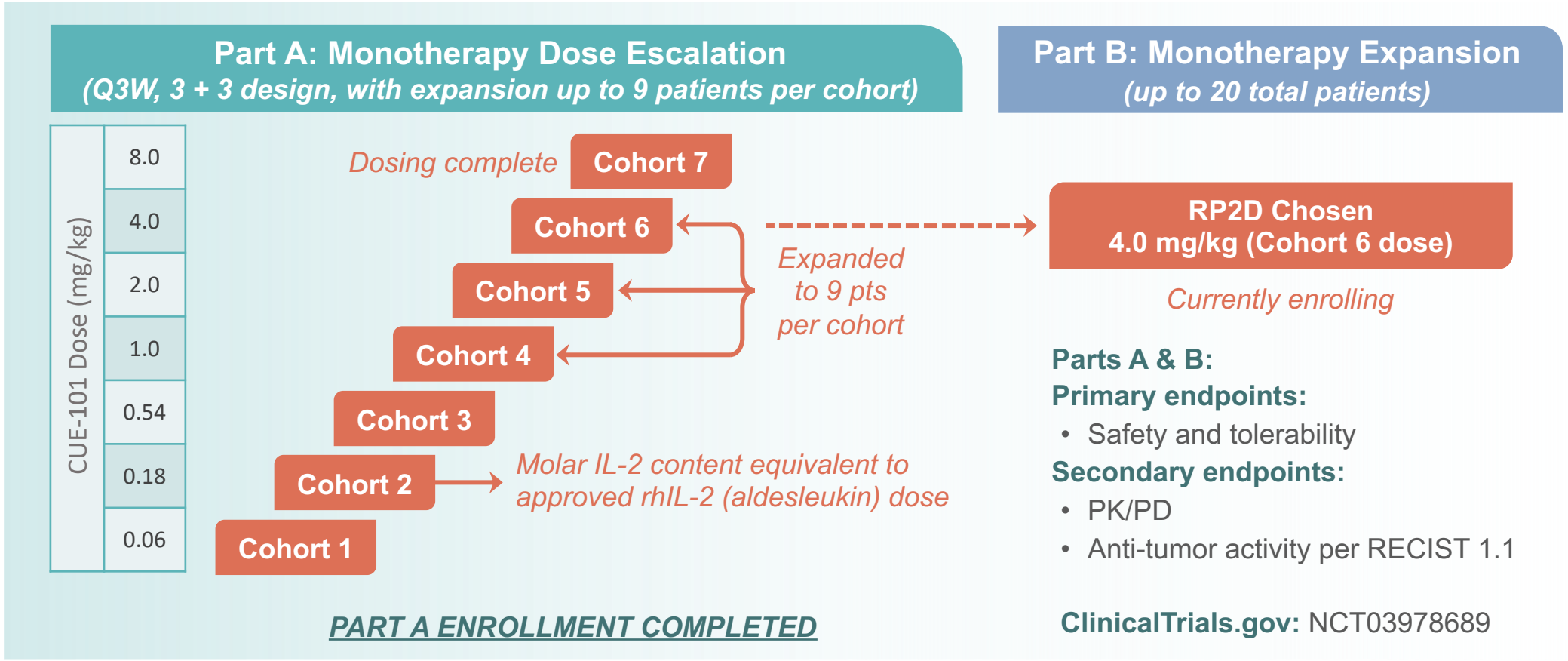
CUE-101: Designed to Selectively Prime & Expand HPV-Specific T cells



- CUE-101 Immuno-STAT addresses an unmet clinical need
- Multiple opportunities within HPV-driven cancers
- Monotherapy in second-line and beyond HPV+ R/M HNSCC establishes proof-of-mechanism for CUE-101 in heavily pretreated challenging patient population
- Supportive monotherapy data establishes foundational position upon which to potentially expand patient reach and therapeutic benefit in additional HPV+ patient populations (e.g., front-line R/M HNSCC with standard of care pembrolizumab)
- Positive clinical data reduces risk of CUE-101 and by implication the IL-2 based CUE-100 series

CUE-101: Ongoing Monotherapy First-in-Human Phase 1 Trial

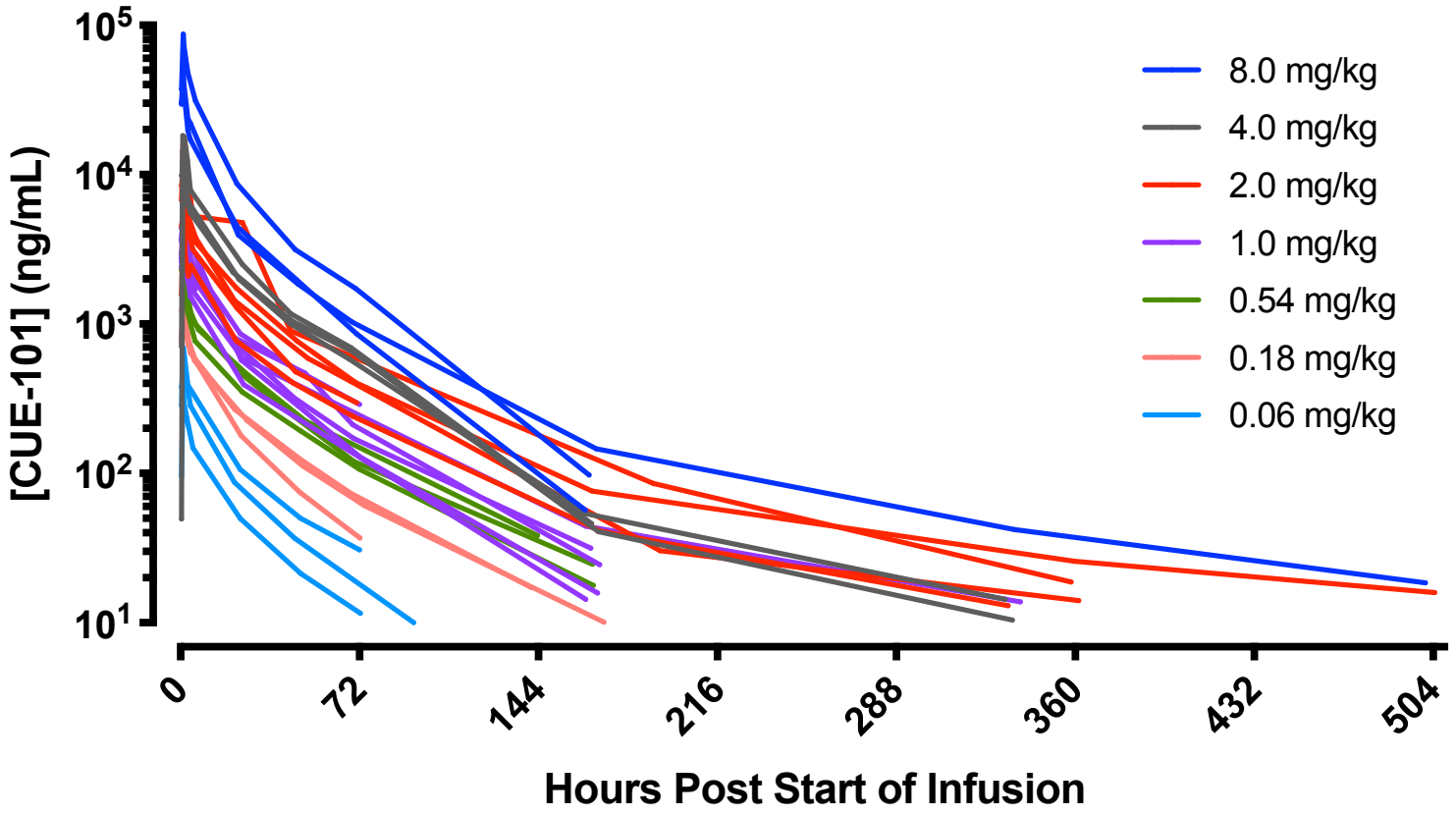
No maximal tolerated dose (MTD) observed in patients dosed up to 8 mg/kg



Abbreviations: CPI, checkpoint inhibitors; HPV, human papilloma virus; PK/PD, pharmacokinetics/pharmacodynamics; Q3W, once every 3 weeks; rhIL-2, recombinant human interleukin-2; RECIST, Response Evaluation Criteria for Solid Tumors; RP2D, Recommended Phase 2 Dose

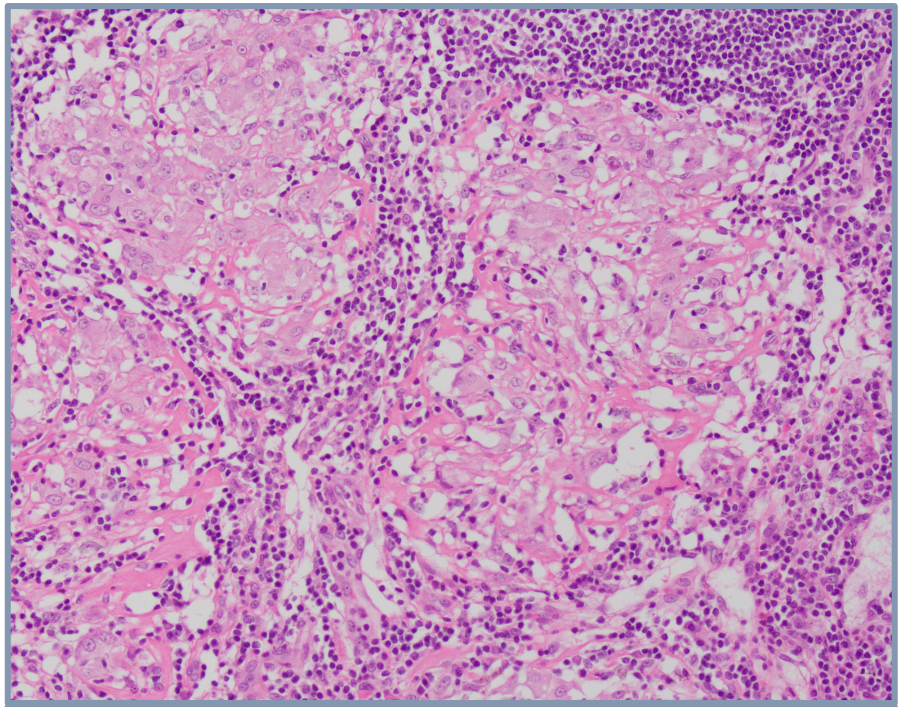
CUE-101: Sustained Exposure Observed with Repeat Dosing

CUE-101 exposures are dose-proportional and comparable upon repeat dosing

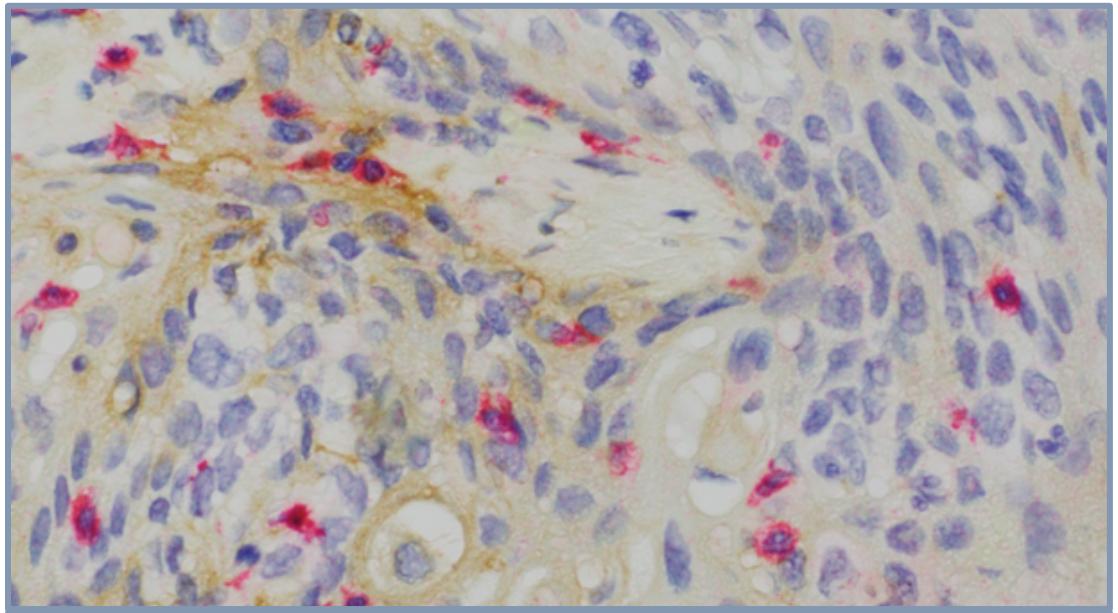


CUE-101: Cohort 4 Case Study – Necrosis and a T cell Infiltrate

Cohort 4 (1 mg/kg) patient was on therapy for over 18 weeks



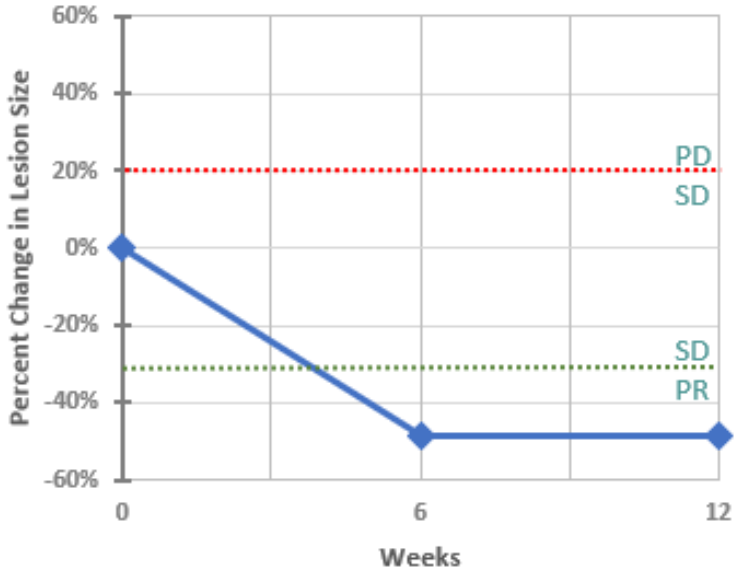
Hematoxylin and Eosin Stain
(Cell nuclei = blue; extracellular matrix and cytoplasm = pink)



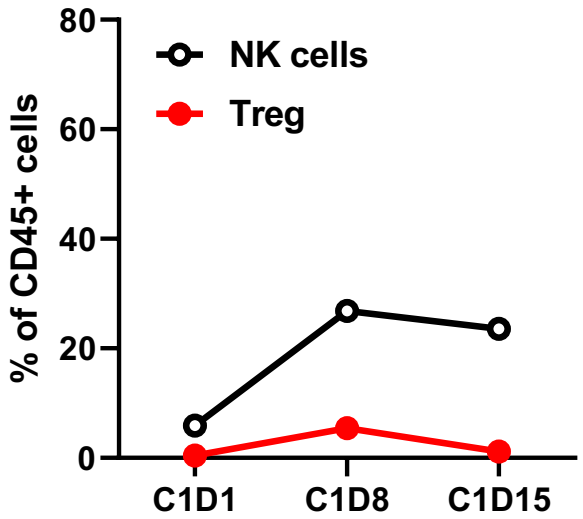
Immunostaining
(Cell nuclei = blue; CD8+ T cells = rose; PD-LI = brown)

CUE-101: Objective Response Observed in Patient with Increased E7-specific CD8+ T cells

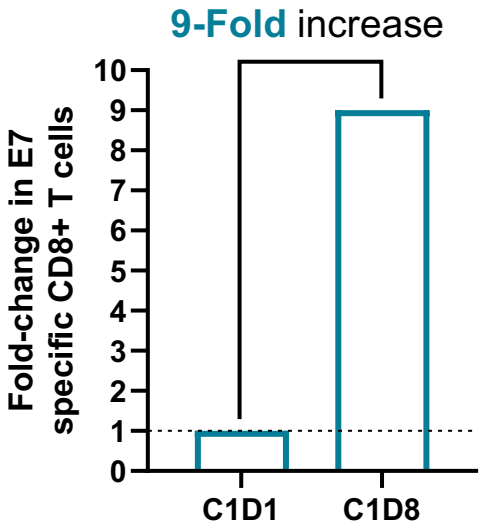
Confirmed PR RECIST 1.1



Two target lesions at baseline
Cohort 6, 4 mg/kg



Pharmacodynamics
Sustained increase in NK cells with a transient increase in Tregs

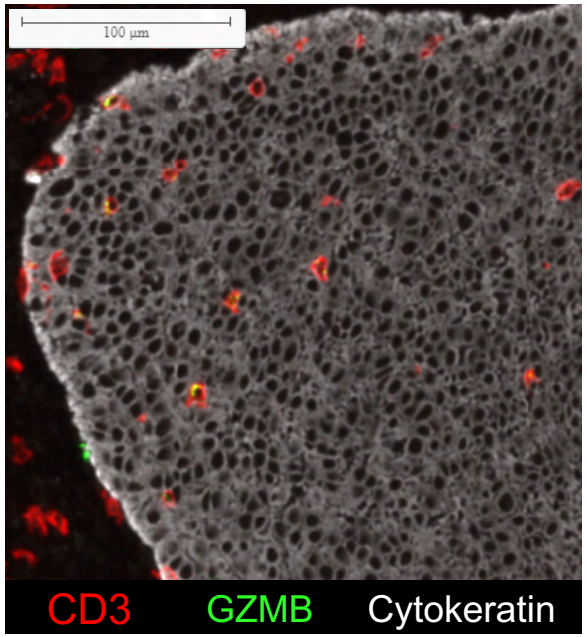


Pharmacodynamics
Increased numbers of E7-specific CD8+ T cells in the blood

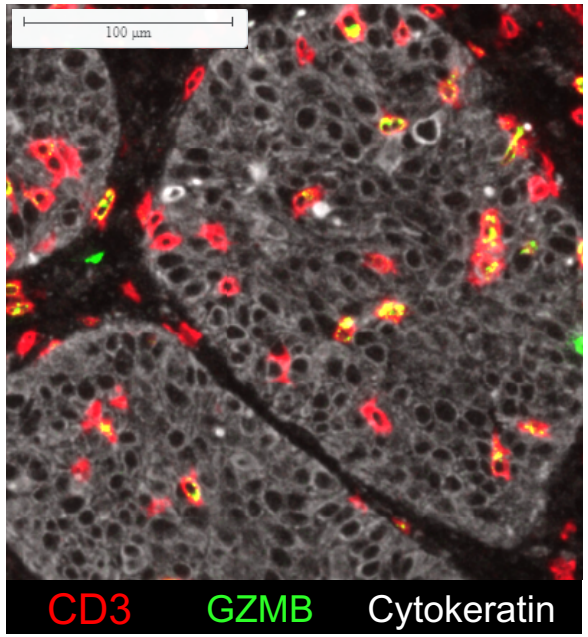
CUE-101 Monotherapy: Increase in Tumor Infiltrating T cells (TILs) Observed by Immunohistochemical (IHC) staining

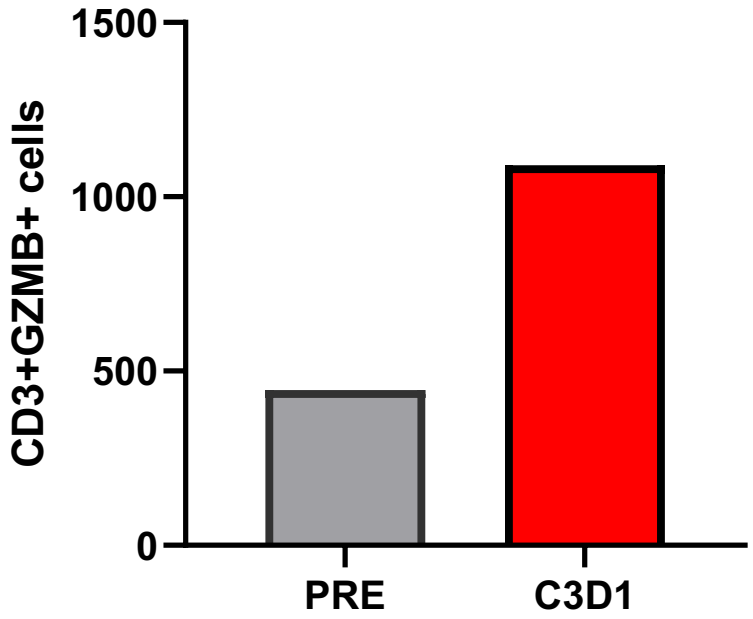
IHC staining reveals increase in TILs (CD3+) and granzyme (GZMB) within a tumor lesion following CUE-101 monotherapy

Pre-dose



Cycle 3 Day 1





CUE-101: Clinical Activity Observations to Date

Part A: Monotherapy Dose Escalation

(Q3W, 3 + 3 design, expansion up to 9 patients per cohort)

- 6 Confirmed SD (stable disease)
- 1 Confirmed PR (partial response)
- No MTD, no DLTs

ENROLLMENT COMPLETED

Part B: Monotherapy Expansion at RP2D

(up to 20 total patients)

- RP2D determined to be 4 mg/kg (Cohort 6 dose)
- 1st Patient dosed in Part B expansion
- Potential monotherapy registration path

Part C: Pembrolizumab Combination Dose Escalation

- Currently enrolling

Part D: Combination Expansion at RP2D Dose

- Expand patient reach to 1st line HPV+ HNSCC
- Enhance therapeutic benefit of CPIs

Neo-adjuvant Trial in Front-line Setting

- Initiate mid-year 2021
- Provide mechanistic insight and further proof-of-concept from tumor microenvironment

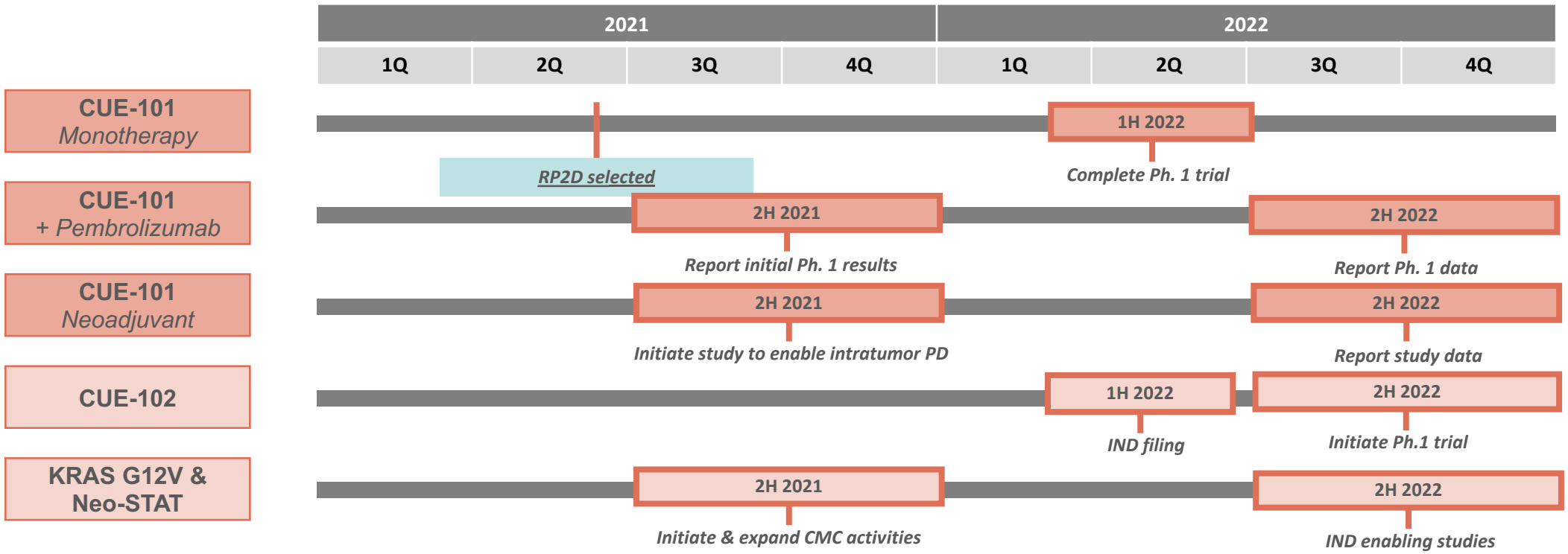
Potential for HPV+ indication expansion

- Cervical, anal, penile, vulvar cancers

Abbreviations: CPI, checkpoint inhibitors; DLT, dose limiting toxicity; HNSCC, head and neck squamous cell carcinoma; HPV, human papilloma virus; MTD, maximum tolerated dose; Q3W, once every 3 weeks; RP2D, Recommended Phase 2 Dose

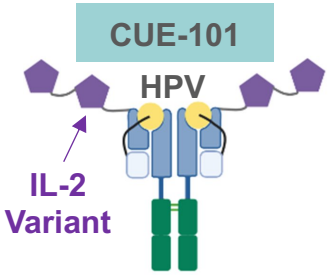
CUE BIOPHARMA

CUE-100 Series: Anticipated Program Milestones



CUE-101: Foundational to the CUE-100 Series

CUE-100 Series Immuno-STATs

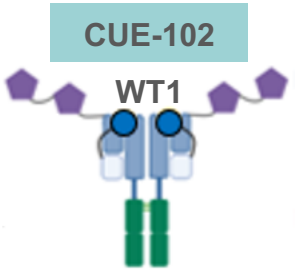


Proof of Concept: HNSCC	
New cases	18,870
Deaths	3,870

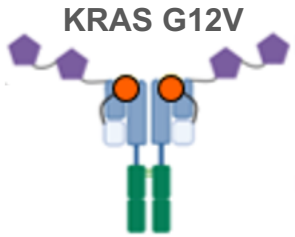
1. 2L+ R/M, monotherapy
2. 1L, Keytruda combination
3. Neoadjuvant, newly Dx

Cervical	
New cases	14,480
Deaths	4,290

Anal, vulvar, penile	
New cases	17,420
Deaths	2,940

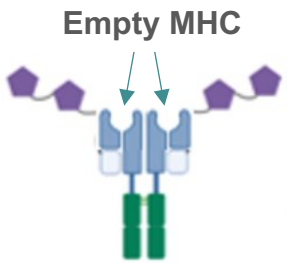


WT1 Overexpression is observed in at least 30 different solid tumor and 6 hematologic malignancies		
	New cases	Deaths
Lung	235,760	131,880
Colon	104,000	52,980
Panc	60,430	48,220
Pros	248,530	34,130
Bladder	83,730	17,200
Ovarian	21,400	13,770
AML	20,240	11,400
#1 NCI Ranked Cancer Vaccine Antigen[1]		



KRAS mutation is a poor prognostic biomarker for several common cancers	
Cancer	Frequency[2]
Panc	90%
Colorectal	40%
NSCLC	20-30%

CUE-100 Series Immuno-STAT Derivatives

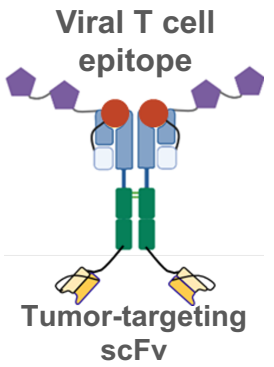


Neo-STATs

Enhances productivity / scale

Address tumor heterogeneity with flexibility in conjugating tumor antigens or neoantigens of interest into the empty MHC peptide binding pocket for personalized cancer therapy

Multiple cancer types



RDI-STATs

Addressing a common tumor escape mechanism: downregulation of MHC is observed in up to 30% of cancers

Anti-viral (e.g., CMV) CD8+ T cells infiltrate tumors

A tumor-targeting scFv linked to the Fc domain tricks an anti-viral CD8+ T cell into killing the tumor cell

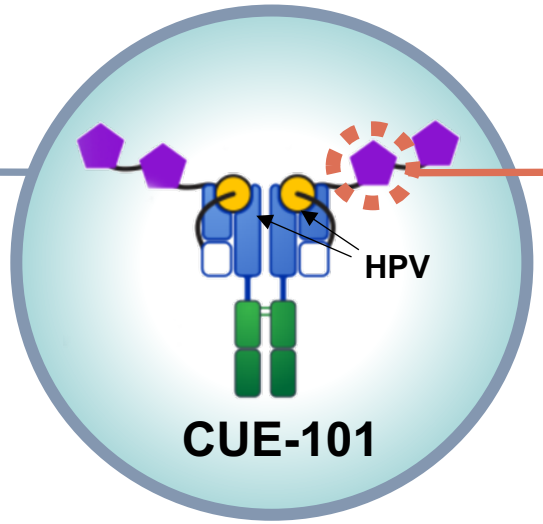
Note: All new cases and deaths figures are from the American Cancer Society. Cancer Facts & Figures 2021. Atlanta: American Cancer Society; 2021.

1. The Prioritization of Cancer Antigens: A National Cancer Institute Pilot Project for the Acceleration of Translational Research. Cheever MA, Allison JP, et al. Clin Cancer Res 15(17):5323–37, 2009.
2. Muñoz-Maldonado C, Zimmer Y, et al. A Comparative Analysis of Individual RAS Mutations in Cancer Biology. Front Oncol 9:1088, 2019.

CUE-101 Experience Enables Broad Opportunities in IO and AI

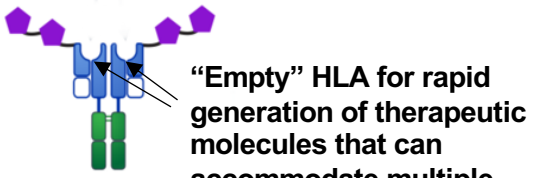
Immuno-oncology

Immuno-STAT Pipeline



Neo-STAT

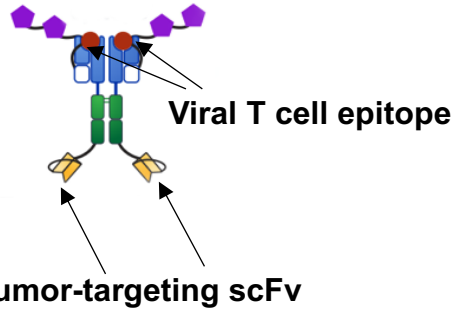
(Addresses tumor heterogeneity)



"Empty" HLA for rapid generation of therapeutic molecules that can accommodate multiple tumor epitopes

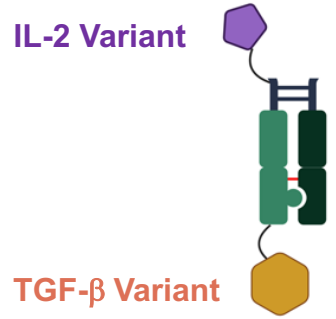
Bispecific RDI-STATs

(Addresses tumor-escape mechanisms)

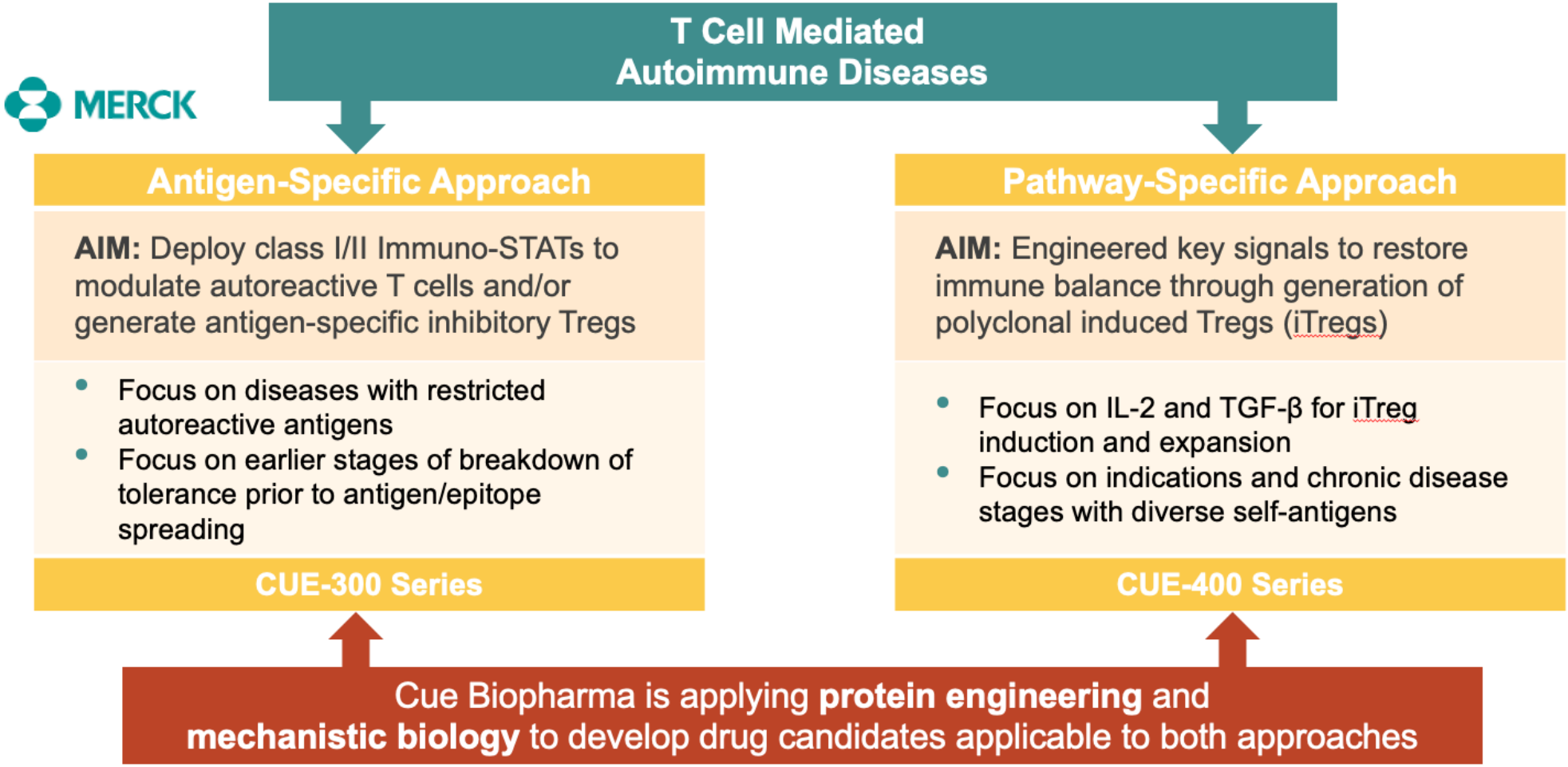


AI & Inflammation

CUE-401: iTreg Inducer



Approaches to Modulate Autoreactive T cell Responses



Immuno-STAT Platforms: Multiple Value Creation Opportunities

We believe our IL-2 based CUE-100 platform, represented by CUE-101 has the potential to be transformative as a breakthrough immunotherapy for cancer

Clinical data to date appears to have reduced the risk of CUE-101's development and, by implication, the CUE-100 series of drug candidates built upon the same IL-2 framework

- **Confirmed PR and 6 confirmed SD** observed to date in the Part A dose escalation study
- **RP2D determined to be 4 mg/kg** (Cohort 6 dose)
- **Part B patient expansion** (up to 20 patients) holds promise of supporting potential registration path in 2L+ HNSCC patients

CUE-100 derivative Neo-STAT and RDI-STAT platforms address tumor heterogeneity and escape mechanisms, respectively, and have next-generational potential in the treatment of multiple types of cancers

- **IND enabling studies** to be initiated in 2022

Cue Biopharma is well positioned to advance to the next stage of its corporate evolution with breakthrough protein engineering technologies for treating cancer and autoimmune diseases

CUE BIOPHARMA

Thank You

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

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