



# Corporate Presentation

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Immune Responses, On Cue™

Nasdaq: CUE

July 20, 2020

# Forward-Looking Statements

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# Corporate Highlights

## Disruptive Platform for T Cell Modulation *In Vivo*

### ***Immuno-STAT & Neo-STAT Platforms***

- Distinct mechanism of action for selective modulation of disease-relevant T cells directly in a patient's body
- Modular therapeutic frameworks targeting cancer and autoimmune disease
- Industry-standard manufacturing, without need for ex vivo manipulation

## Focused Execution Against Platform Validation

- CUE-101 in Phase 1 for R/M HPV+ head and neck cancer
  - ❖ Preliminary clinical data presented in 1H20; additional data in 2H20
- Immuno-STAT platform modularity demonstrated with peptides (WT1 and KRAS) and HLA (A02, A11, A24)
  - ❖ Preclinical data with CUE-102 (WT1/A02 & A24) presented in 1H20
- Neo-STAT capability enhances R&D efficiency and expands the landscape of clinical utility

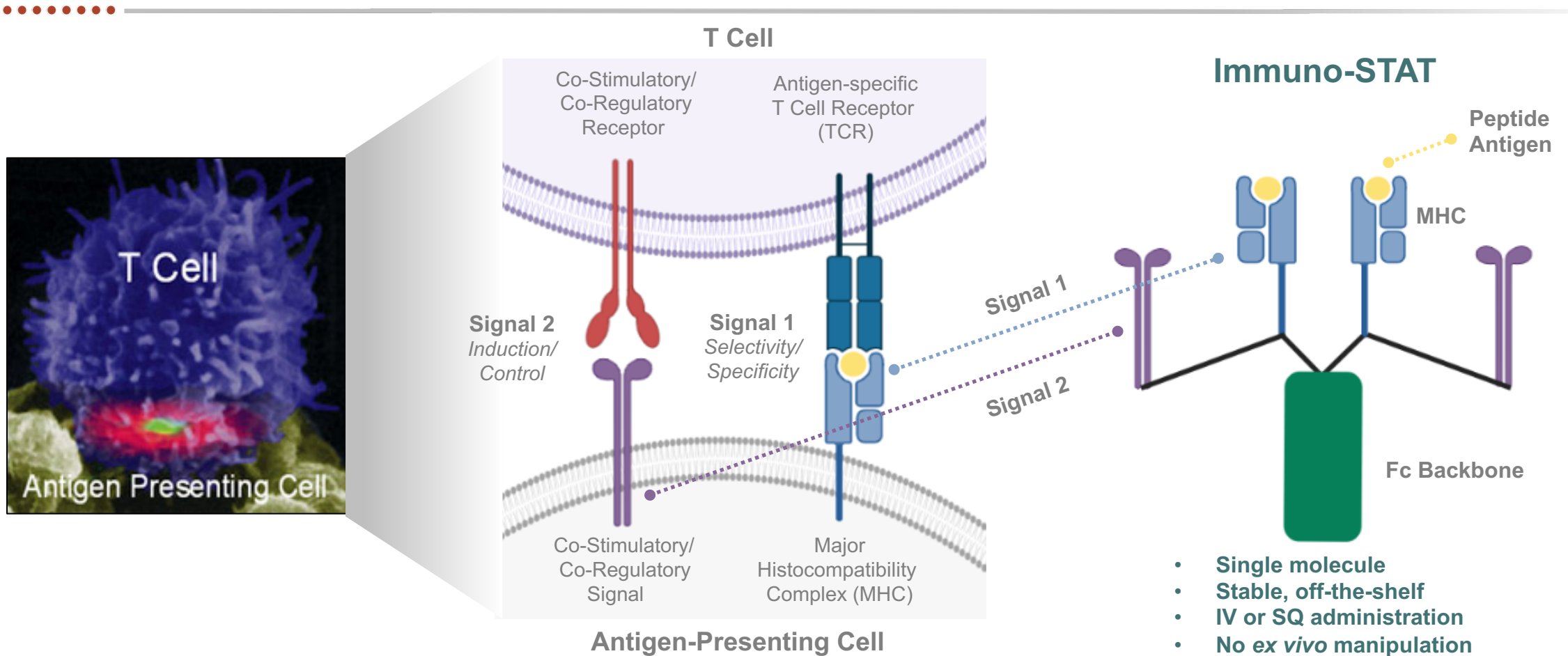
## Strategic Partnerships to Accelerate Expansion

- LG Chem collaboration to expand IL-2 based CUE-100 series in immuno-oncology
- Merck collaboration to establish proof of mechanism for CUE-300 series Immuno-STAT platform in autoimmune disease
  - ❖ Preclinical data with CUE-301 presented in 1Q20

**Strong financial position supports key readouts from ongoing CUE-101 clinical study and further expansion of Immuno-STAT platform**

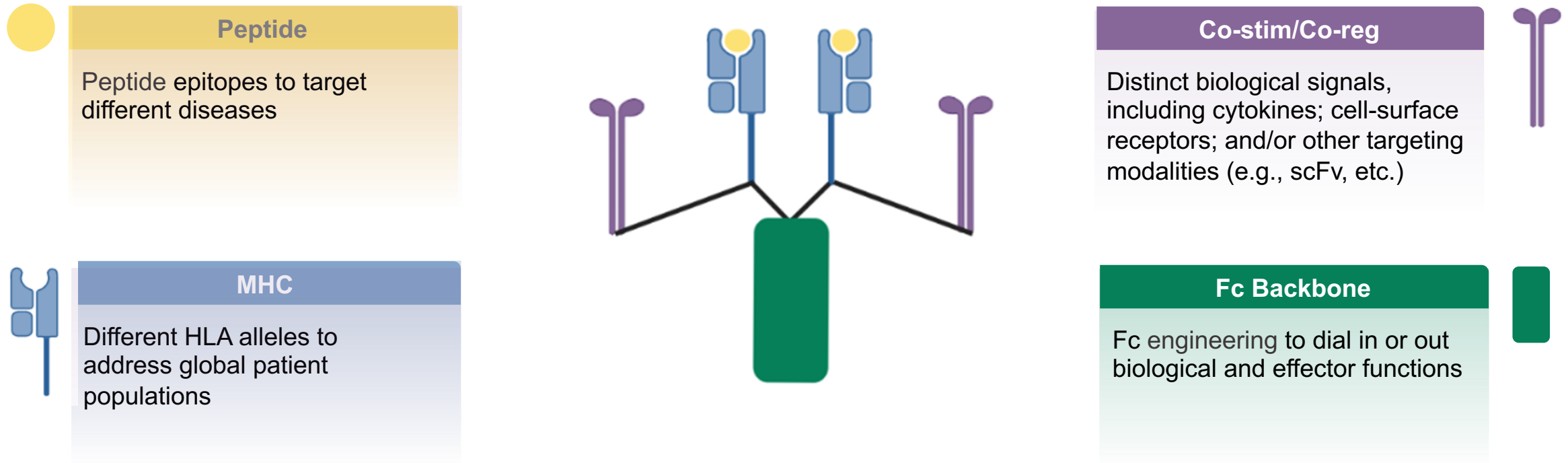


# Emulating Nature's Cues to Selectively Modulate T Cells



Rationally engineered Immuno-STAT biologics selectively target and modulate the activity of disease-relevant T cells

# Immuno-STAT Modularity: 4 Interchangeable Modules



Combinatorial diversity presents potential to generate therapeutic molecules for a broad set of diseases and patient populations

# Pipeline



## TARGET SELECTION

## PRE-CLINICAL

## PHASE 1

## LATE CLINICAL

## PARTNER

**CUE-100**  
IL-2

**CUE-101 (HPV E7 / A02)**

**CUE-102 (WT1 / A02)**

**CUE-102 (WT1 / A24)**

**CUE-103 (Undisclosed)**

**KRAS / A11**

**CUE-201 (Undisclosed)**

**CUE-200**  
CD80 &  
4-1BBL

**CUE-301 (Proins / DR4)**

**CUE-302 (Undisclosed)**

**CUE-300**  
PD-L1 &  
Undisclosed



*Asia Rights to  
CUE-101, CUE-  
102, and CUE-103*



*Collaboration  
for Autoimmune Disease*

CUE-100: Human papilloma virus (HPV)-positive cancers expressing HPV E7 protein (e.g., head and neck cancer)

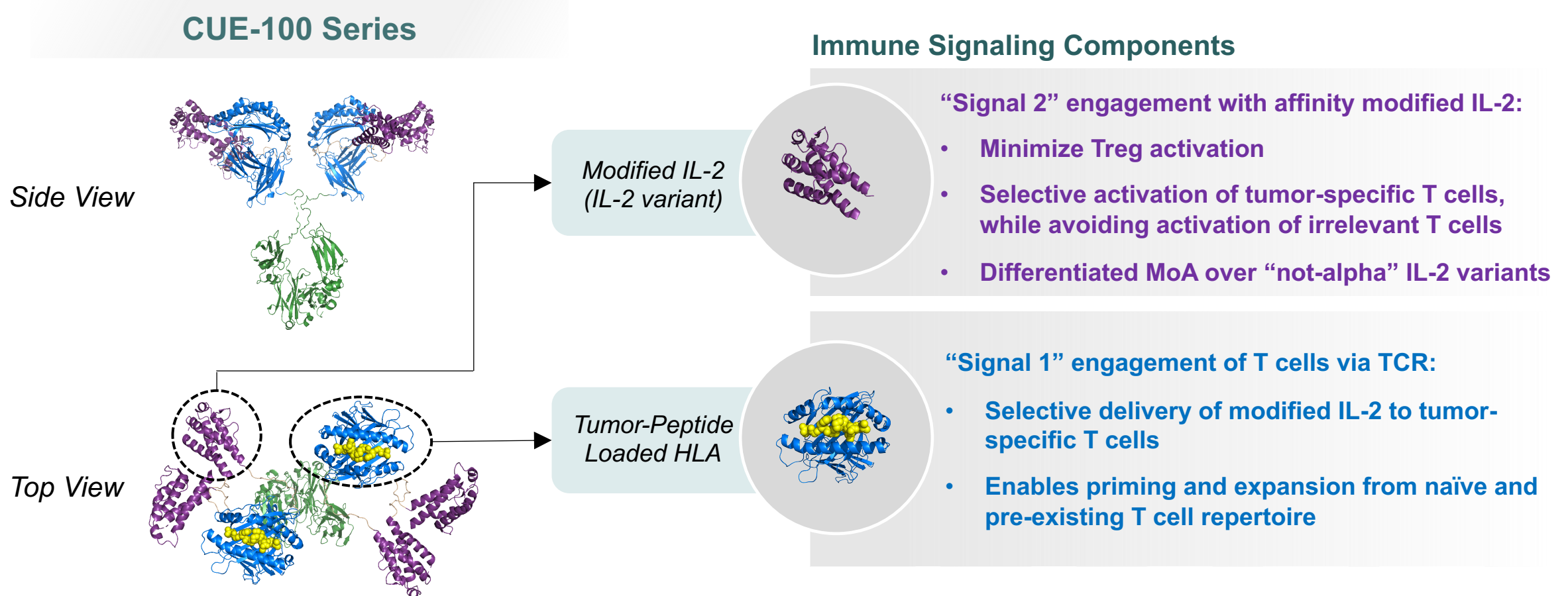
CUE-102: Wilms Tumor 1 (WT1) positive cancers (e.g., leukemia and multiple solid cancers)

CUE-301: Type 1 diabetes with autoreactive T cells targeting proinsulin producing beta cells in the pancreas

KRAS is an oncogene and when mutated it is overexpressed and associated with many cancer types



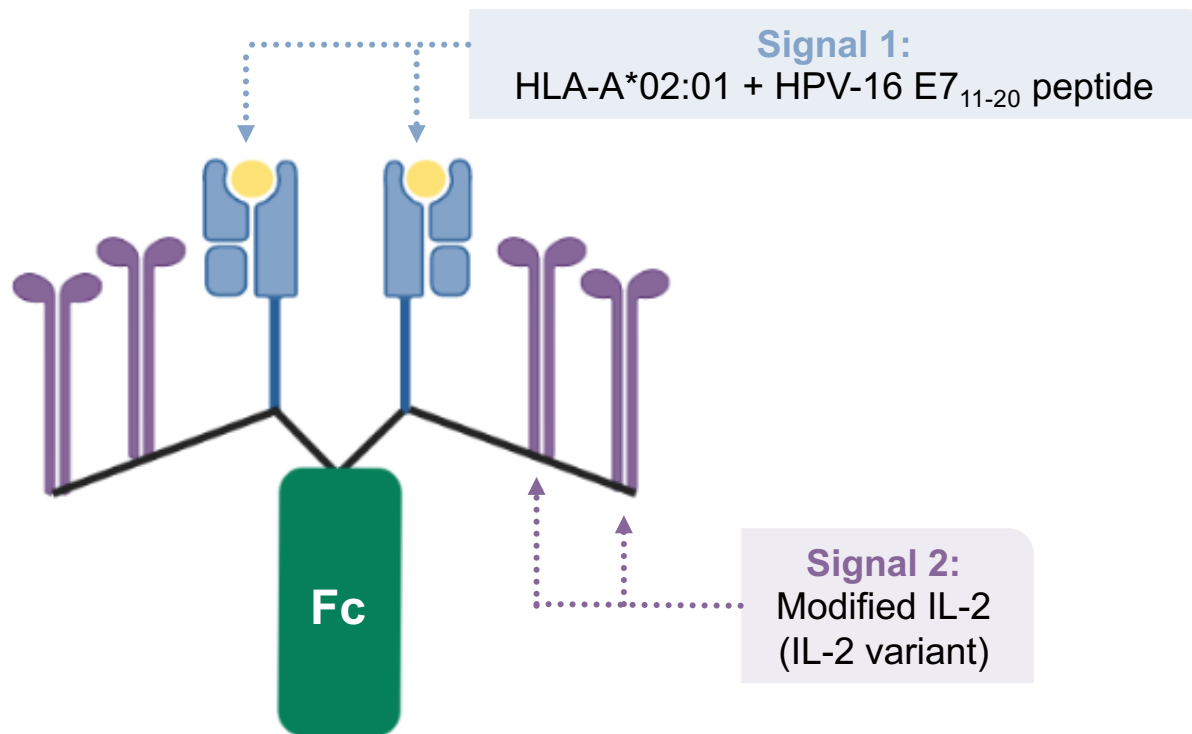
# CUE-100 Series: Exploiting IL-2 via Rational Protein Design



Therapeutic framework is not dependent on barriers of antigen processing & presentation, and is designed to avoid systemic immune activation

# CUE-101: Lead Clinical Candidate for HPV-Driven Malignancies

## CUE-101 Immuno-STAT Design



## Clinical Rationale

- CUE-101 is designed to selectively prime and expand HPV-specific T cells in vivo
- HPV is recognized as a growing driver of head and neck cancer and is now responsible for over 70% of oropharyngeal cancers in the US and EU
- Despite treatment with current standards of care, more than 50% of patients with advanced disease will experience recurrence with significant quality of life impacts
- The CUE-101 clinical development strategy builds upon robust translational preclinical data and patient stratification

# CUE-101: Phase I Clinical Development Network

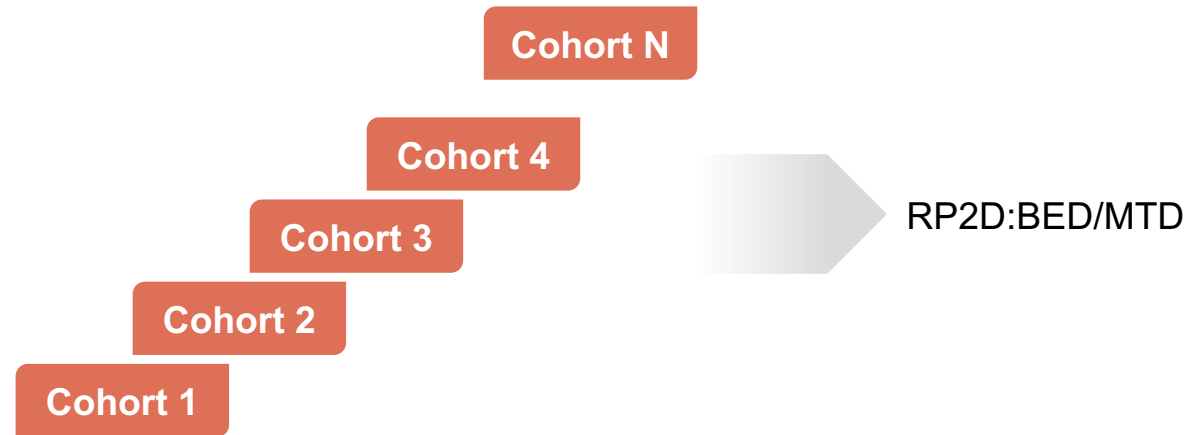
- **Emory Winship Cancer Institute:** Nabil Saba
- **Karmanos Cancer Institute:** Elizabeth Heath and Ammar Sukari
- **MD Anderson Cancer Center:** Bonnie Glisson
- **MGH/Harvard and Dana Farber Cancer Institute:** Sara Pai and Lori Wirth
- **Moffitt Cancer Center:** Christine Chung
- **Memorial Sloan Kettering Cancer Center:** Lara Dunn
- **Stanford Cancer Center:** A. Dimitrios Colevas
- **University of Arizona Center:** Julie Bauman
- **University of Michigan Rogel Cancer Center:** Frank Worden
- **University of Washington Fred Hutch Cancer Center:** Cristina Rodriguez
- **Vanderbilt-Ingram Cancer Center:** Jill Gilbert and Mike Gibson
- **Washington University Siteman Cancer Center:** Doug Adkins
- **Yale Cancer Center:** Barbara Burtness

Cue has engaged a network of nationally recognized clinical investigators and 13 Phase I sites are now open



# CUE-101: Ongoing First-In-Human Study

## Part A: Monotherapy Dose Escalation



## Part B: Monotherapy RP2D Expansion

Late Line Accelerated Monotherapy  
Approval Opportunity in H&N

- **Eligibility**

- Part A & B: HPV+ H&N Cancer, R/M,  $\geq 2^{\text{nd}}$  Line

- **Design** (CUE-101 Q3W)

- Part A: Dose Escalation (3+3 Pts)
- Part A: PD & Activity Expansion (Up to 9 Pts)
- Part B: Dose Expansion (10-20 Pts at RP2D)

- **Objectives**

- Primary: Safety and Tolerability
- Secondary: PK/PD, Anti-Tumor Activity

- **Biomarkers** (Pre/Post CUE-101 Dose)

- HPV E7-specific CD8+ T cell counts
- HPV E7-specific CD8+ T cell functionality
- Immunophenotyping, cytokine release, and TCR sequencing

- **NCT03978689**



# CUE-101: Part A Dose Cohorts

Cohort	CUE-101 Dose	CUE-101 Dose Relative to Approved Proleukin Dose (0.037 mg/kg)	CUE-101 IL-2* Content (nmol/kg)	CUE-101 IL-2 Content Relative to Approved Proleukin Dose (2.4 nmol/kg)
Cohort 1 ✓	0.06 mg/kg (starting dose)	~ 1.6x	1.1	~ 0.46x
Cohort 2 ✓	0.18 mg/kg	~ 4.9x	3.4	~ 1.4x
Cohort 3 ✓	0.54 mg/kg	~ 14.6x	10.3	~ 4.3x
Cohort 4 ✓	1 mg/kg	~ 27.0x	19.1	~ 8.0x
Cohort 5	2 mg/kg	~ 54.0x	38.2	~ 16.0x
Cohort 6	4 mg/kg	~ 108.0x	76.4	~ 32.0x
Cohort 7	8 mg/kg	~ 216.0x	152.9	~ 64.0x

Note: Check mark indicates patient(s) have been enrolled at dose level; enrollment for cohort 4 ongoing.

\*Modified IL-2 to abrogate binding to IL-2R alpha and reduce binding affinity to IL-2R beta



# CUE-101: Safety & Activity Observations from Cohorts 1 – 4



## Safety

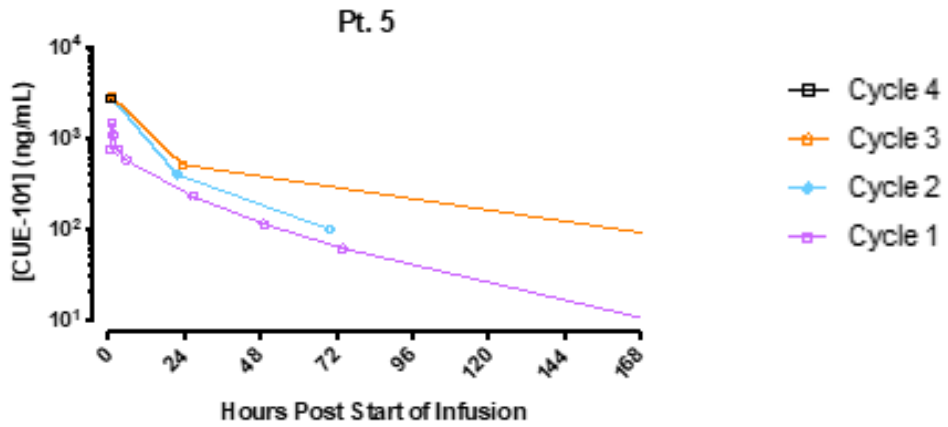
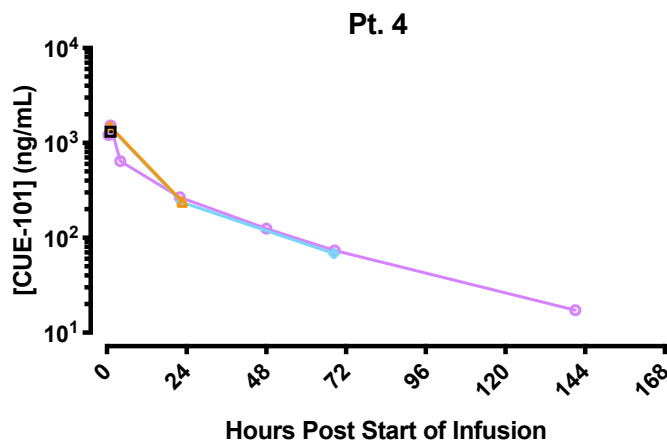
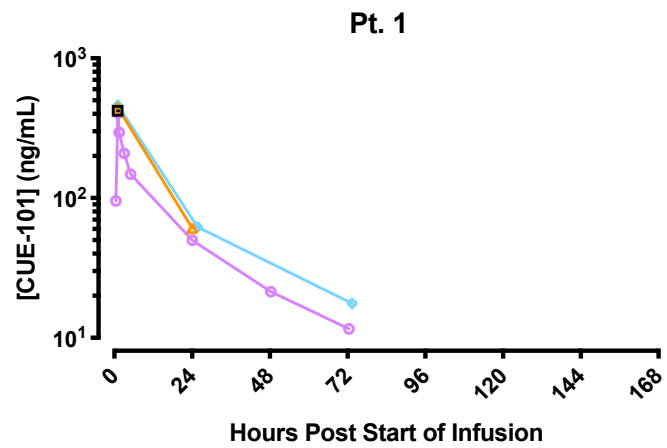
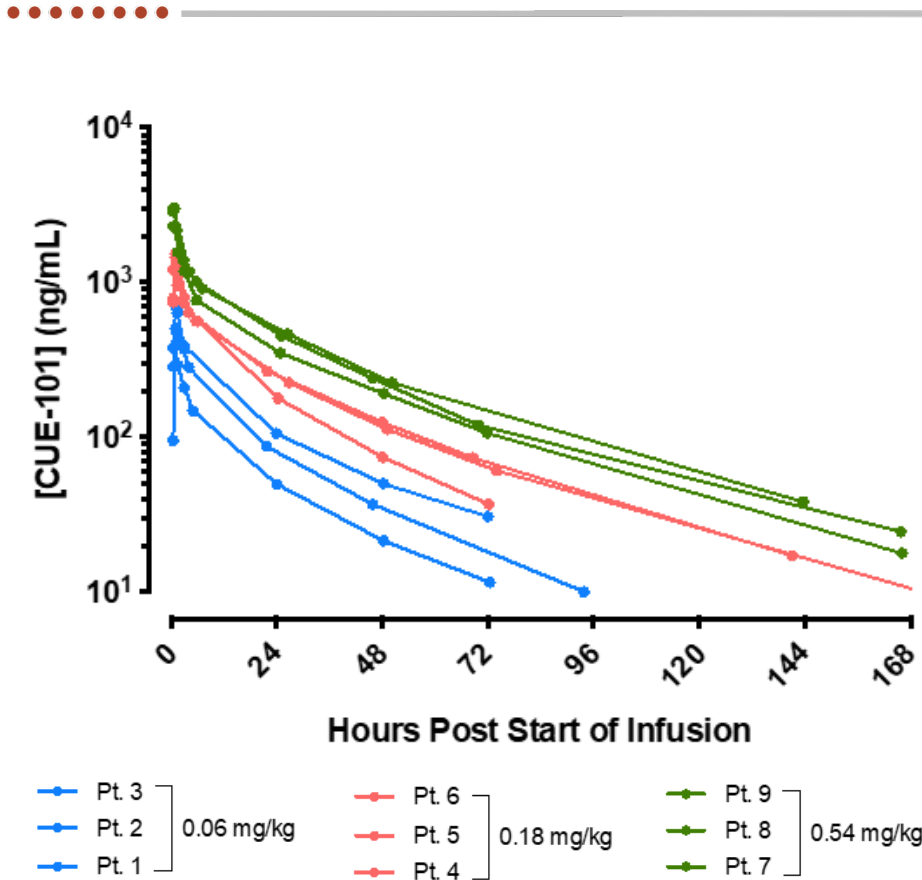
- Multiple patients receiving multiple injections indicates favorable safety and tolerability profile
- No drug-related DLTs in cohorts 1-3
- Cohort 4 expanded by 3 additional patients per protocol due to 1 patient experiencing Grade 3 adverse event (AE) that was designated as a possible drug-related DLT
  - Patient remains on study and received their next scheduled dose after AE resolution
- No patient discontinuations on trial due to adverse events

## Activity

- PK data from the first three cohorts indicates:
  - *Exposure in-line with preclinical projections*
  - *Dose-proportional drug exposure*
  - *Comparable exposures observed upon repeated administration*
- PD data indicates early signals of selective T cell expansion
- Preliminary evidence that CUE-101 is clinically active



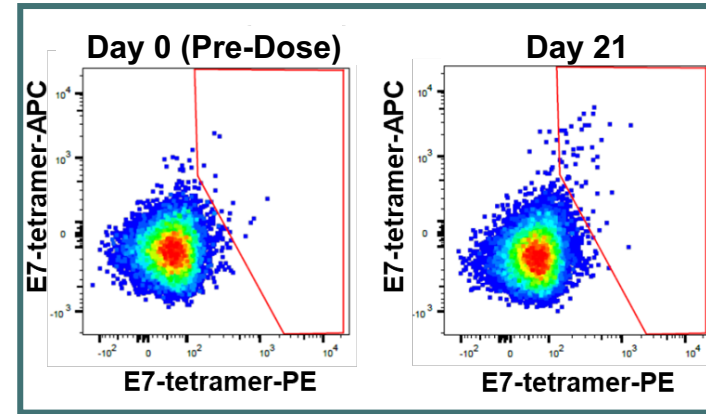
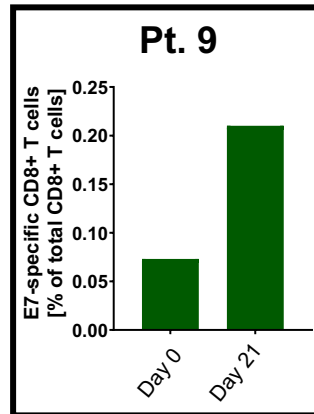
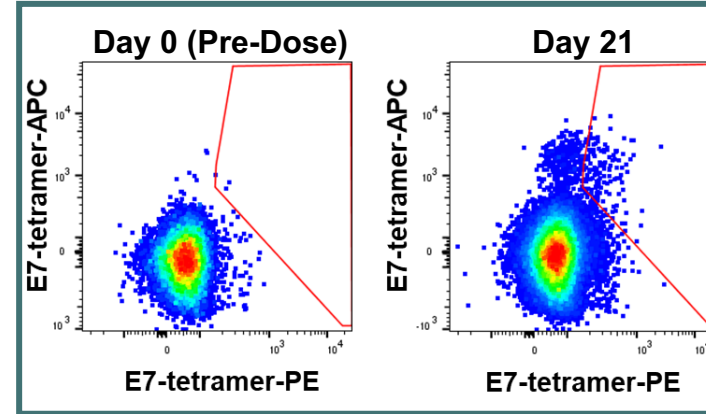
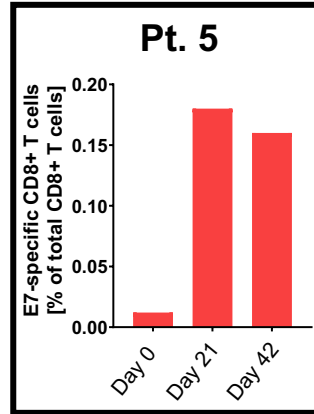
# CUE-101: Dose-Proportional & Repeat Exposures from Cohorts 1 - 3



CUE-101 exhibits dose-proportional increases in exposure in line with projections from non-clinical studies and comparable exposures upon repeated administration



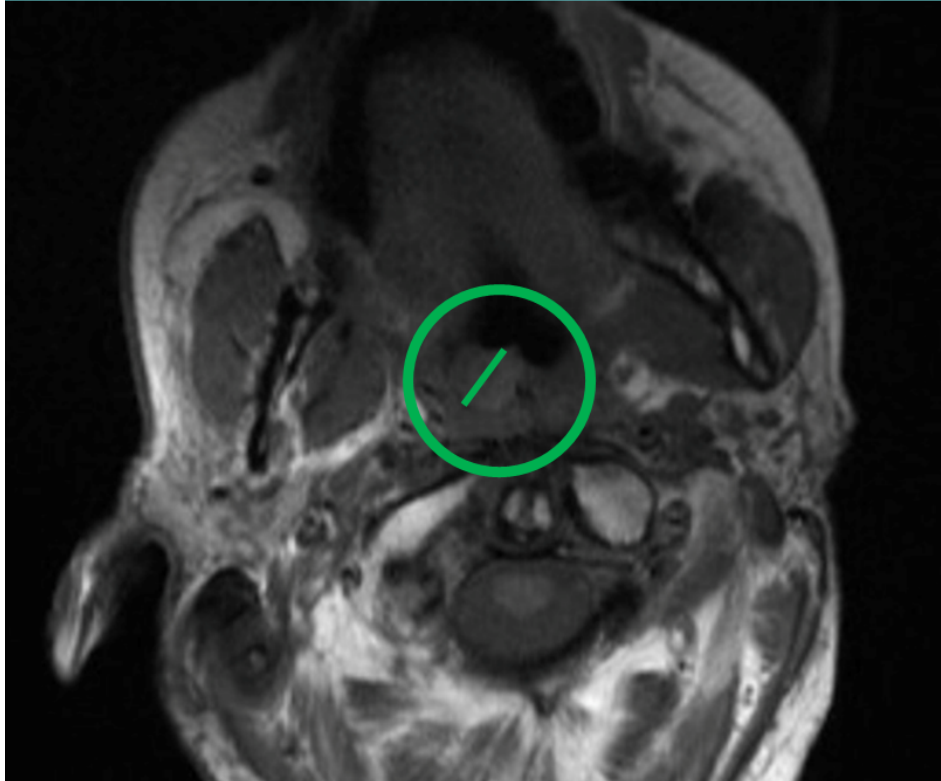
# CUE-101: Expansion of E7-specific T Cells



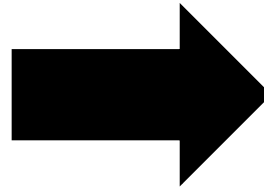
Preliminary evidence of expansion of E7-specific T cells observed in several patients

# CUE-101: Cohort 2 Patient Case Study

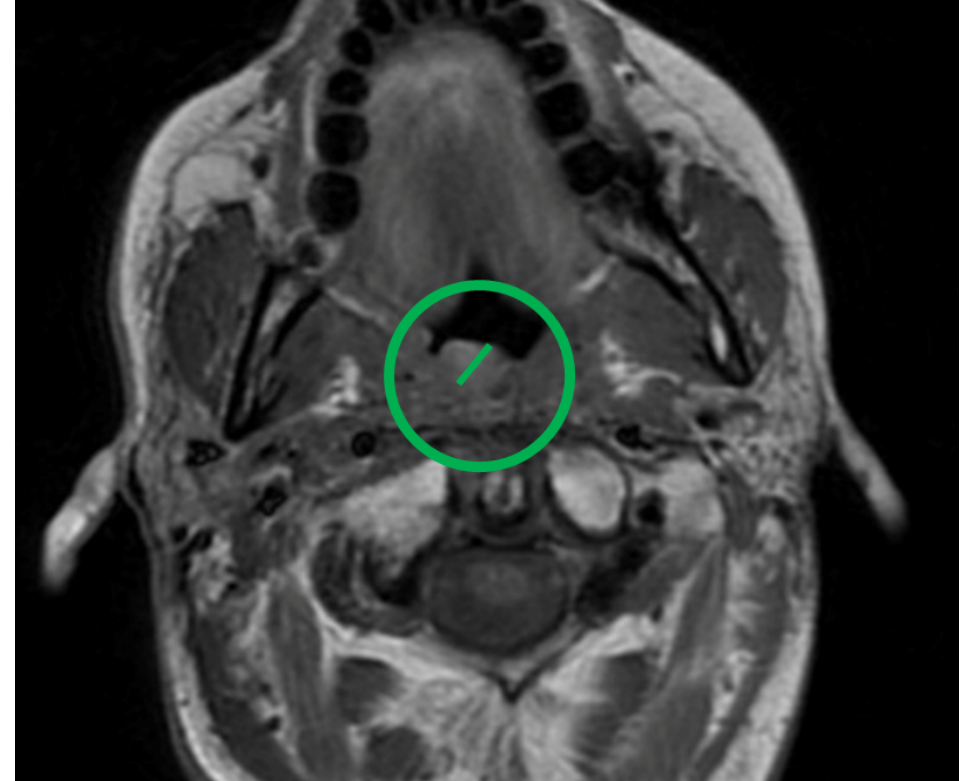
Day 0: Baseline Tumor



Scan at day 42  
(after 2 cycles  
of CUE-101)  
indicates  
reduction of  
>1cm target  
lesion



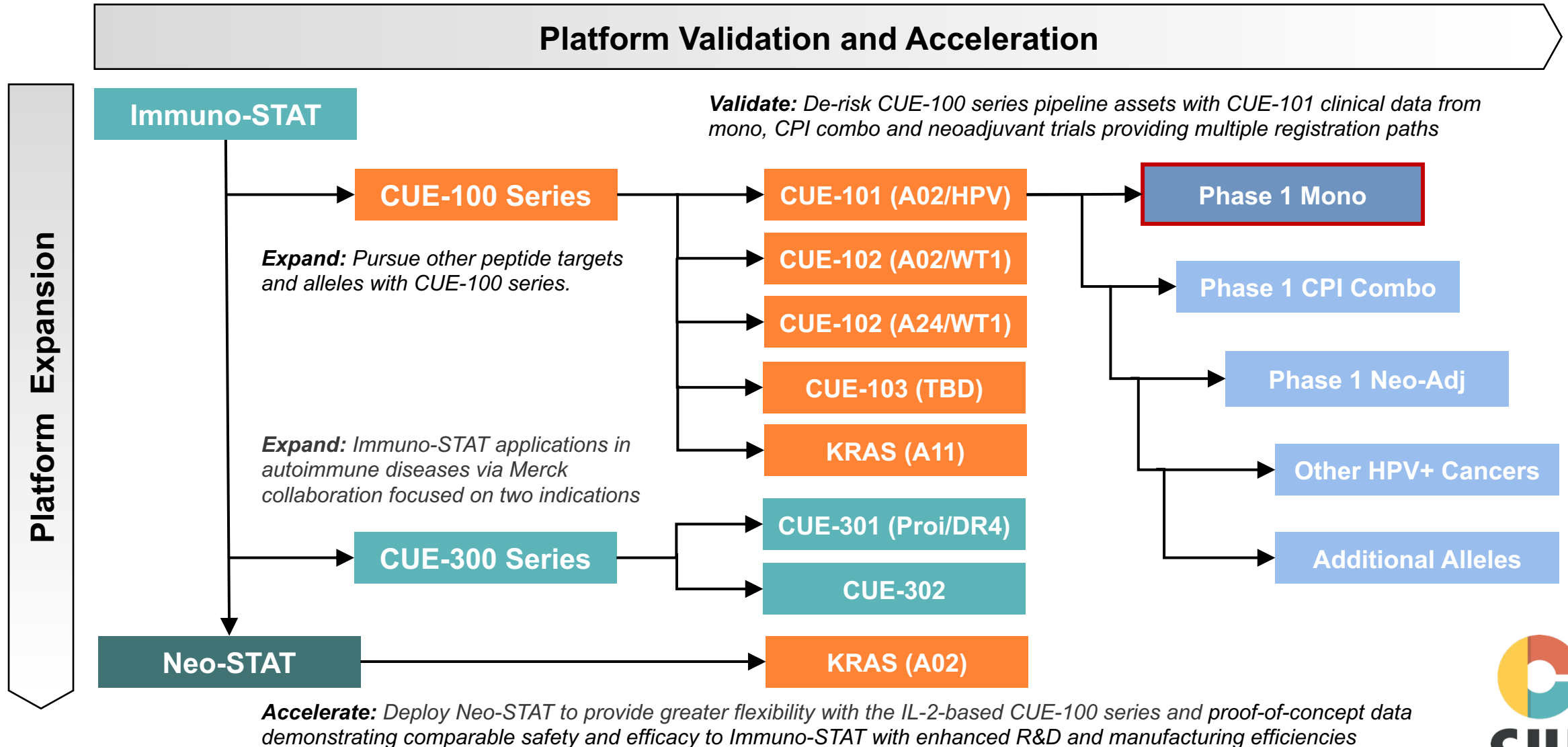
Day 42: 2 Cycles of CUE-101 Monotherapy



At day 84 the repeat scan showed sustained regression of the target lesion,  
and at that point the patient was confirmed as stable disease

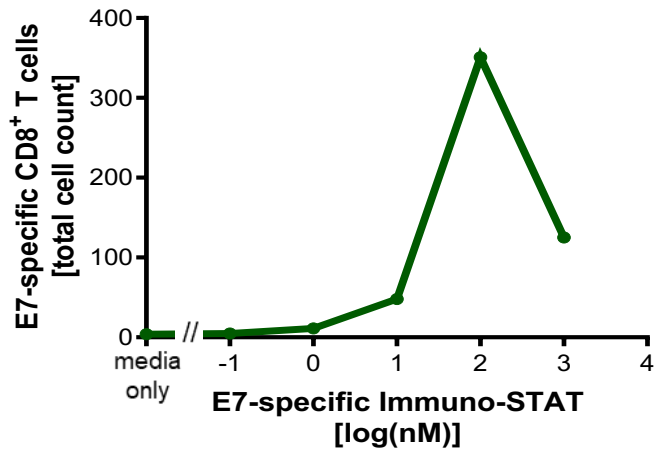
*Patient had received multiple lines of therapy, including checkpoint inhibition*

# Corporate Development and Growth Strategy

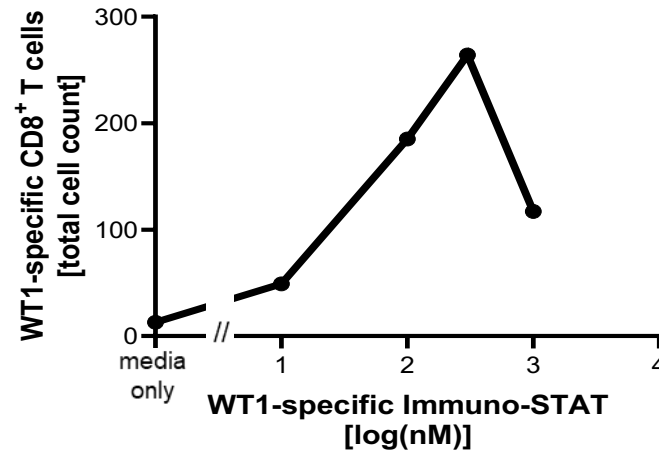


# Immuno-STATs Demonstrate Selective T Cell Expansion

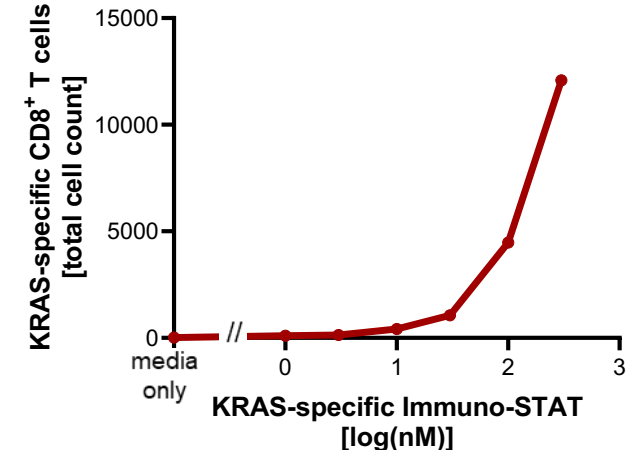
## HPV (CUE-101)



## WT1 (CUE-102)



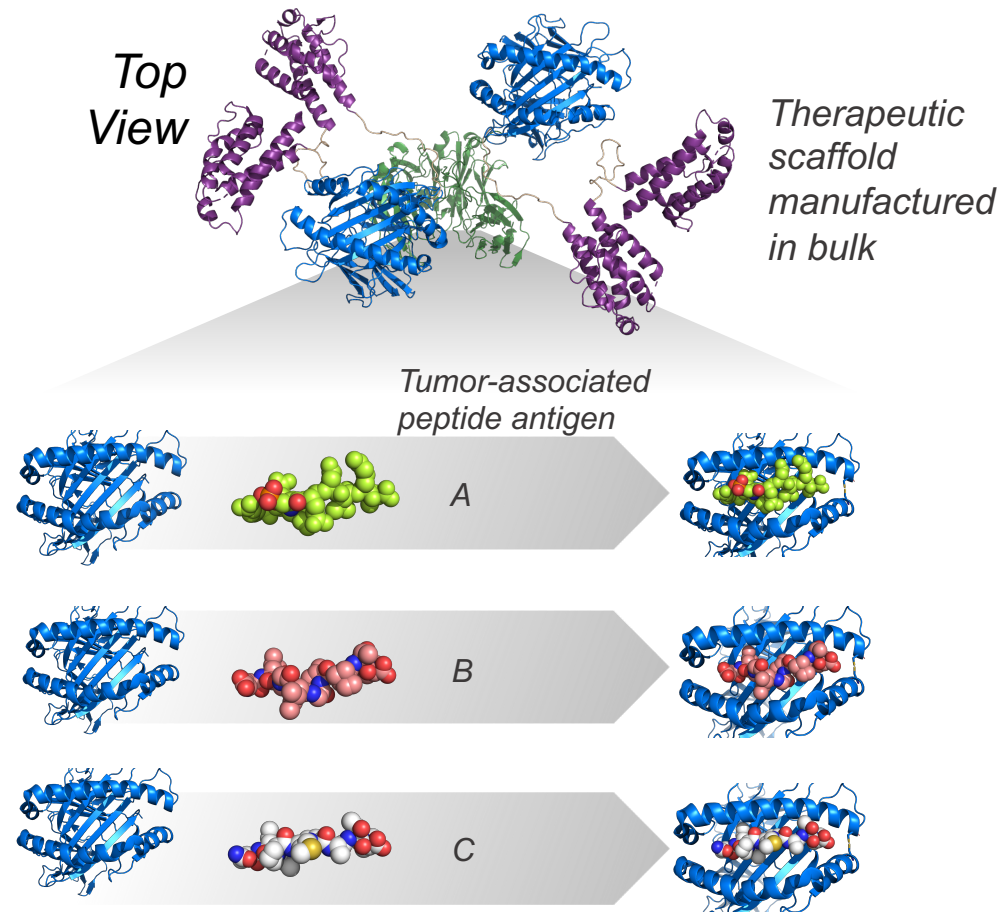
## KRAS IST



Emerging data from CUE-102 (WT1) recently presented at NYAS Frontiers in Cancer Immunotherapy and AACR Annual Meeting II

# Neo-STAT: Next-gen Evolution of the Immuno-STAT Framework

## CUE-100 Neo-STAT

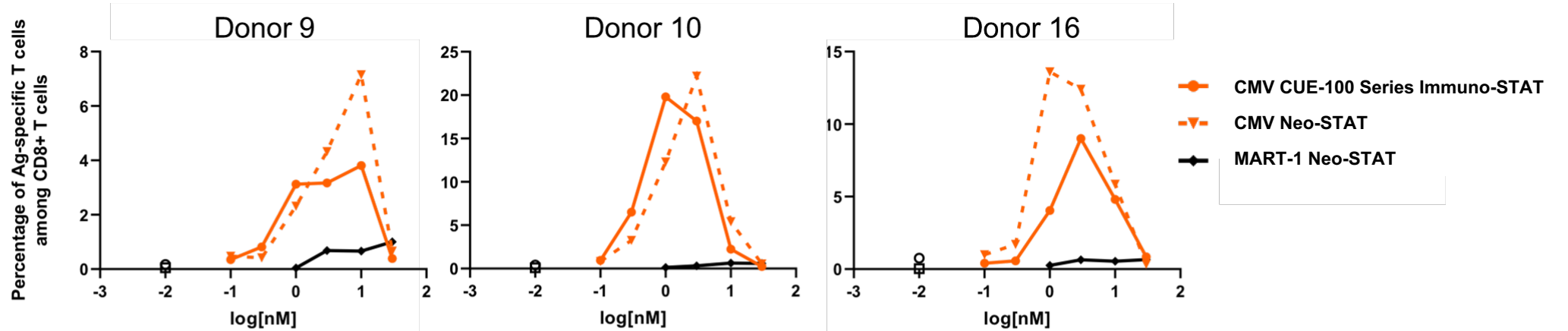


Therapeutic scaffold receptive for chemical conjugation of peptides that potentially:

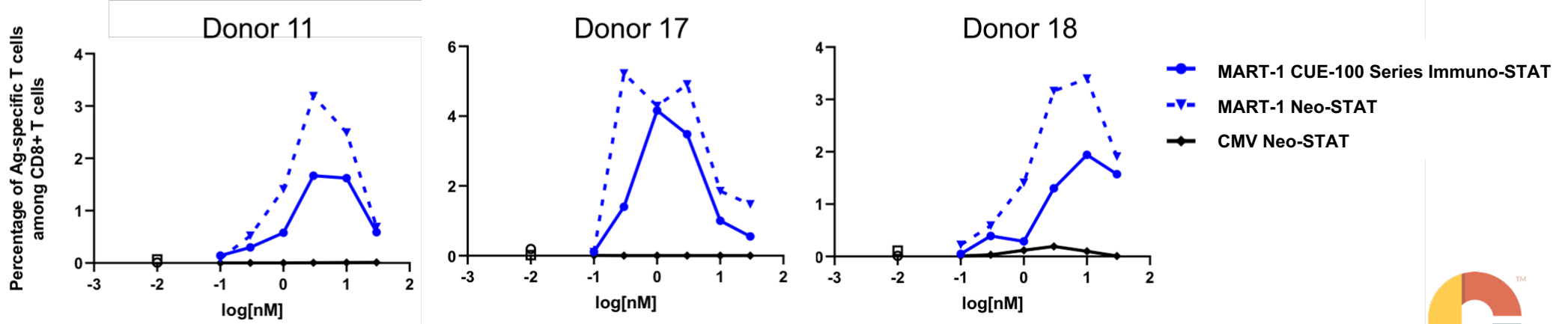
- **Increases R&D efficiency** and reduces cost of the generation of clinical grade material on the CUE-100 framework
- **Enables targeting of multiple tumor antigens** including post-translationally modified peptides and neo-antigens for personalized therapy

# Primary Human T Cell Expansion: Neo-STAT = Immuno-STAT

CMV  
Responsive  
Donors



MART-1  
Responsive  
Donors



# Corporate Development Strategy

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## Validate

- Continue to generate clinical metrics for CUE-101 demonstrating safety, tolerability and clinical activity to de-risk CUE-101, CUE-100 series, as well as Immuno-STAT framework
- Establish therapeutic synergy with checkpoint inhibition through clinical collaboration with Merck to assess CUE-101 in combination with Keytruda in the front-line setting for HPV+ H&N Cancer

## Expand

- Pursue additional targets (i.e., WT1, KRAS) and alleles (i.e., A11, A24) with CUE-100 series and establish preclinical datasets demonstrating selective T cell expansion and activation
- Expand Immuno-STAT applications in autoimmune diseases via Merck collaboration focused on two indications

## Accelerate

- Provide proof of concept data supporting the biological activity of molecules generated via the Neo-STAT platform, and comparability to Immuno-STAT format
- Deploy Neo-STAT to enhance productivities, efficiencies, and provide greater flexibility with the IL-2-based CUE-100 series



# Key 2020 Milestones

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- 1 Additional PK/PD results from the Phase 1 CUE-101 clinical trial in **2H20**
- 2 Clinical responses from the Phase 1 CUE-101 clinical trial via RECIST criteria in **2H20**
- 3 Initiate CUE-101 combination trial with Keytruda in 1L SCCHN in **2H20**
- 4 Initiate and extend IND-enabling activities for CUE-102 in **2H20**
- 5 Select target for CUE-103 in **3Q20**
- 6 Demonstrate Neo-STAT manufacturability and efficiencies in **2H20**
- 7 Identify potential clinical candidates in collaboration with Merck in **2H20**

**Key objectives met in 2019 and early 2020 have set the stage for data flow from multiple programs in the remainder of 2020**





# Thank you

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## Immune Responses, On Cue™

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