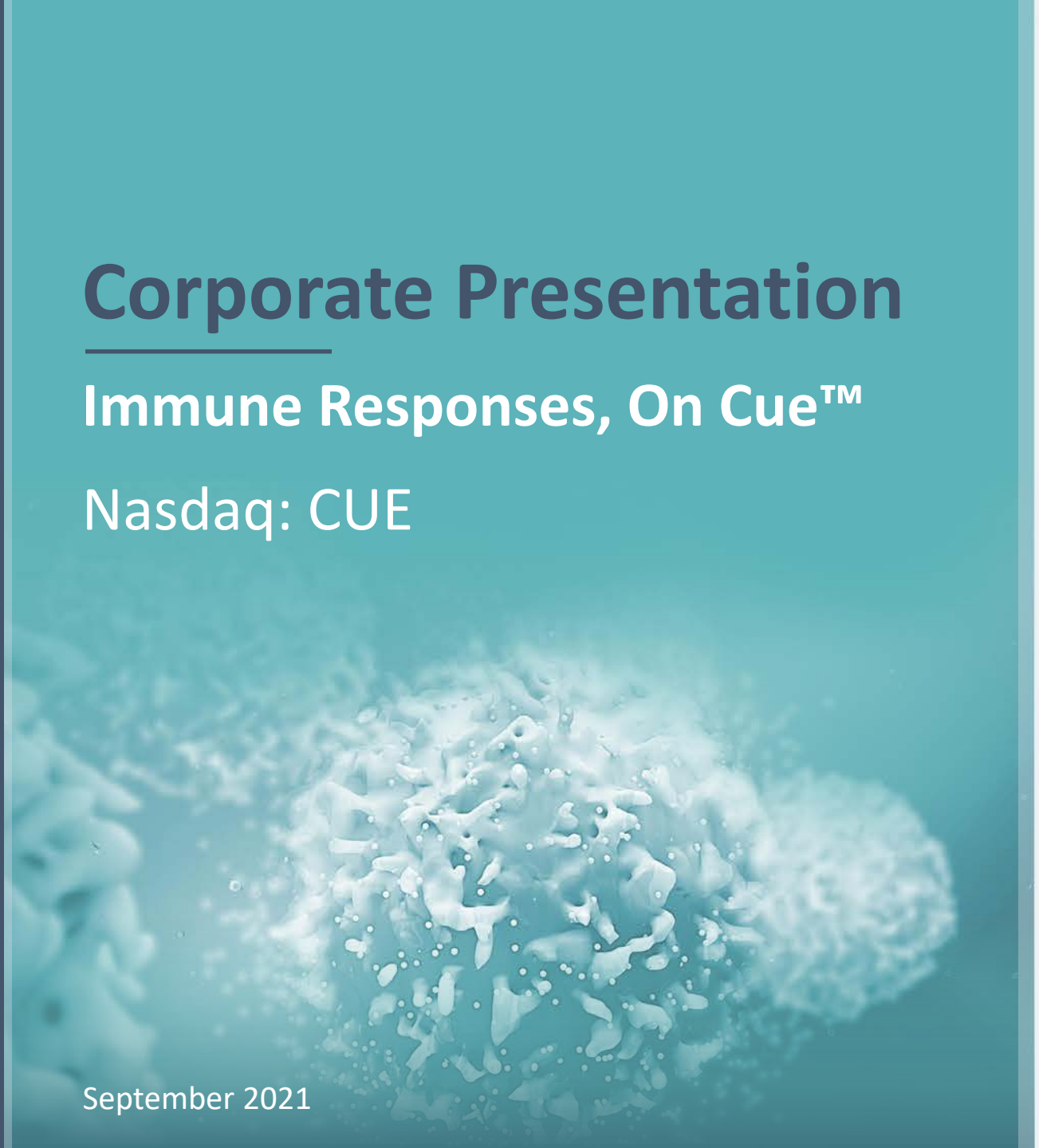
Corporate Presentation

Immune Responses, On Cue™

Nasdaq: CUE



September 2021

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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

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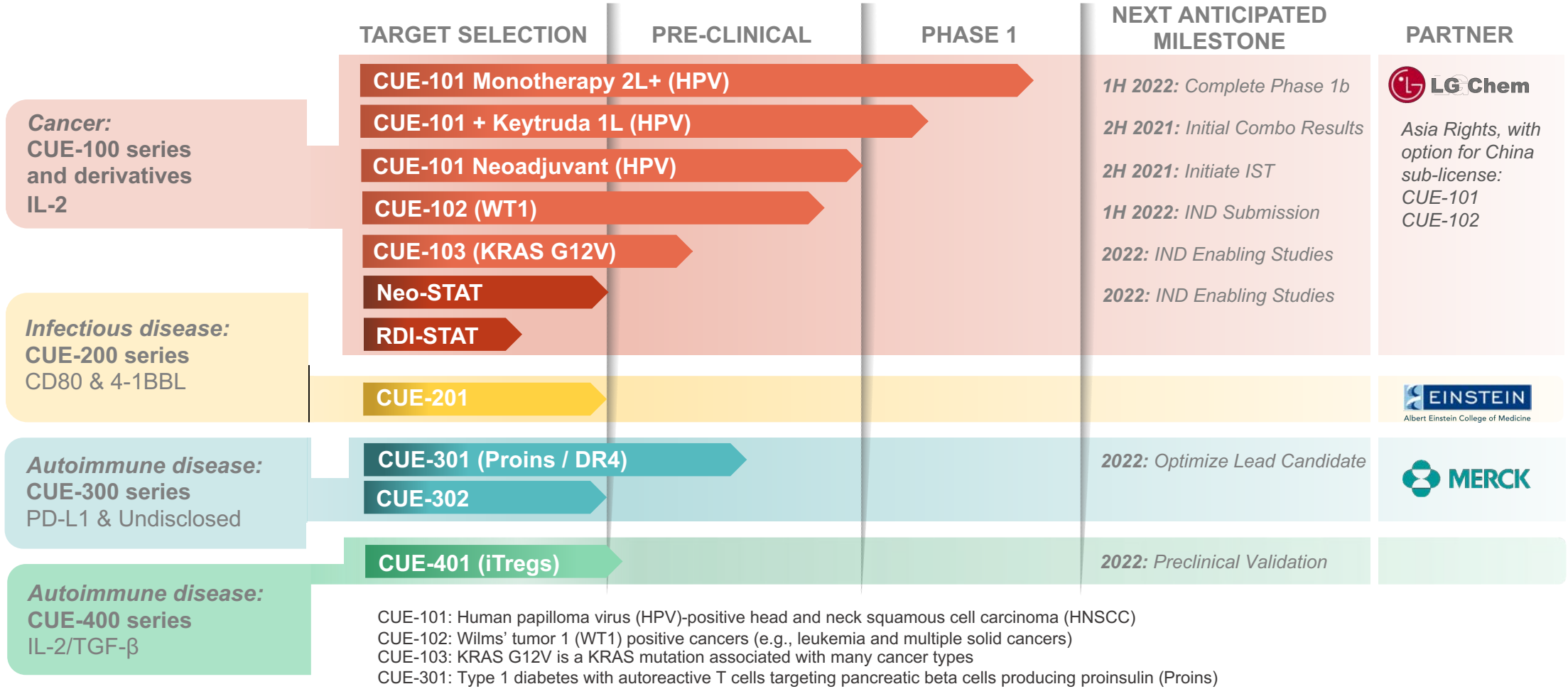
Cue Biopharma Drug Product Candidate Pipeline



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-103: KRAS G12V is a KRAS mutation associated with many cancer types
CUE-301: Type 1 diabetes with autoreactive T cells targeting pancreatic beta cells producing proinsulin (Proins)
CUE-401: Rheumatologic and gastrointestinal autoimmune/inflammatory disorders, GvHD
IST: Investigator-sponsored trial

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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 both cytotoxic T cells and Tregs – leading to severe toxicity

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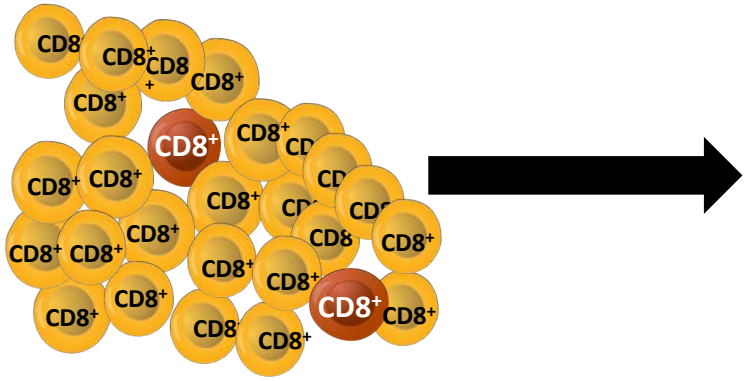
IL-2 Therapy Challenges: Non-selective T cell Activation = Poor Tolerability and Extremely Narrow Therapeutic Window

Wild Type (WT) IL-2 or IL-2 Variants

Examples

- **WT IL-2** *(Proleukin®)*
- **"Not-alpha" IL-2 variants**
- **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)*

Lack of Selectivity for Tumor-specific CD8+ T cells



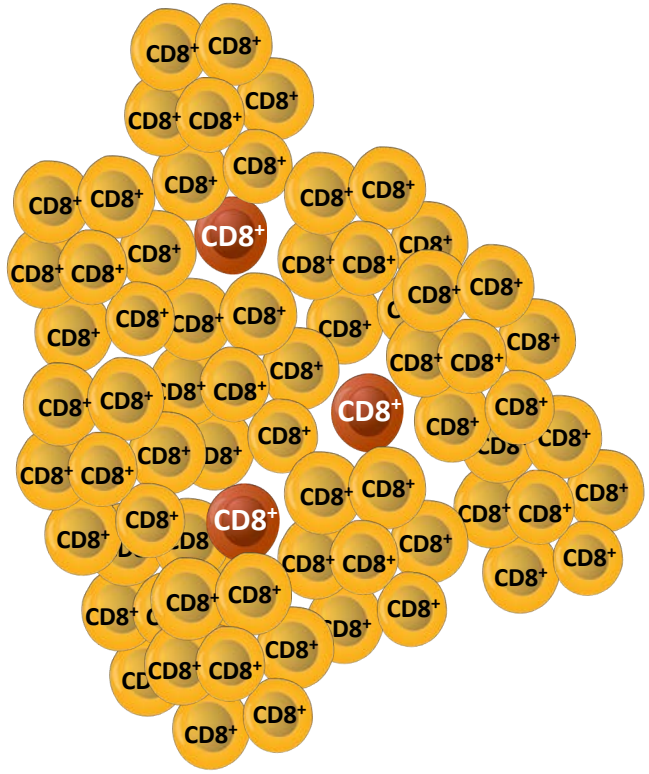
Considerations and Challenges

- **Vast majority of T cells are *NOT* tumor-specific**
- **Need for IL-2 selectivity for tumor-specific T cells**
- **Activation of Tregs**
- **Toxicities (VLS, CRS etc.)**

TUMOR-SPECIFIC CD8+ T CELL

NON TUMOR-SPECIFIC CD8+ T CELL

Non-specific Activation of ALL CD8+ T cells



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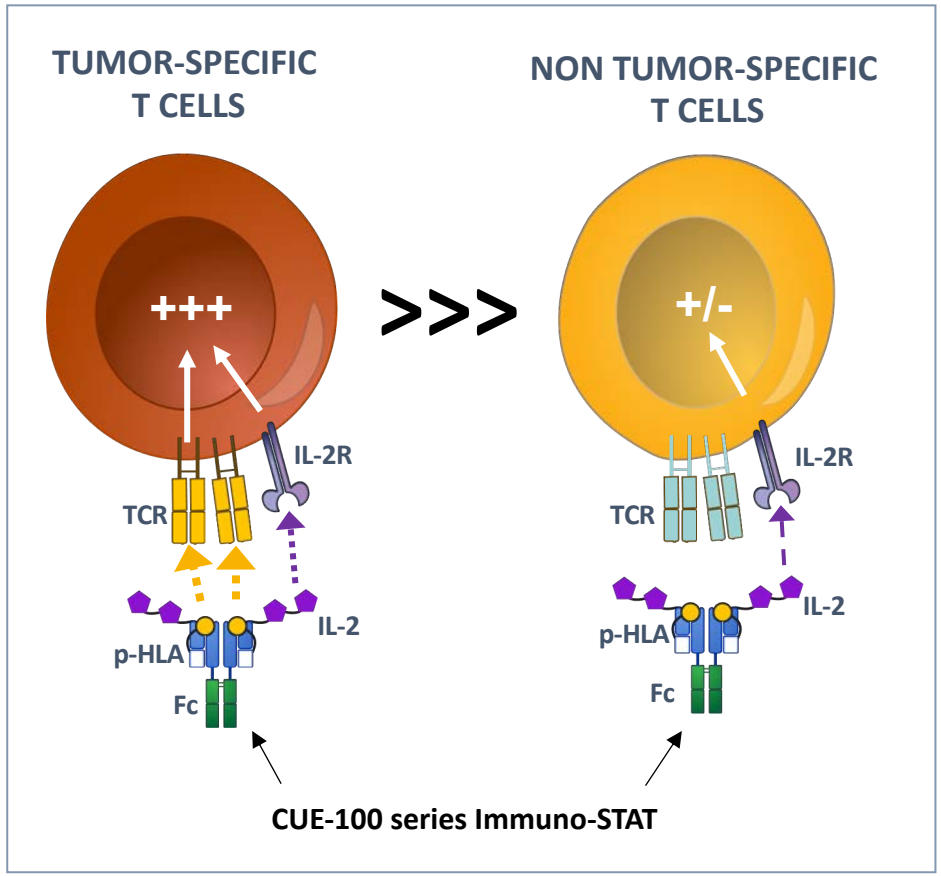
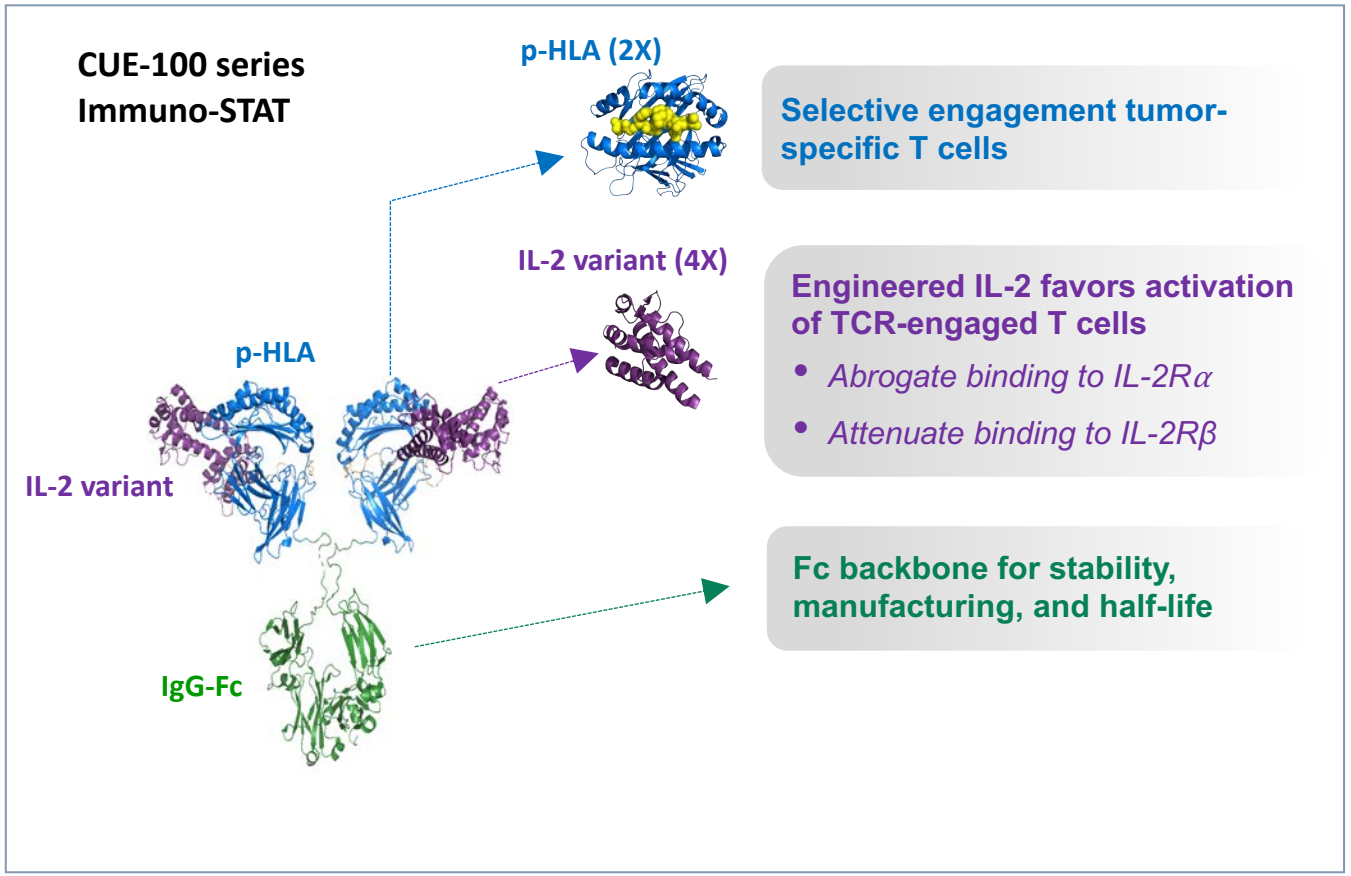
A superior therapeutic strategy would selectively and specifically modulate only disease-relevant T cells, while preserving patient safety and restoring the therapeutic capacity of the patient's immune system.

This is the core foundational principle that underscores our approach with the Immuno-STAT biologics platform

CUE-100 Series: Designing an IL-2 Variant in Context of T Cell Receptor (TCR) Engagement

Molecular structure exploits concurrent TCR and IL-2R engagement to activate tumor-specific CD8+ T cells





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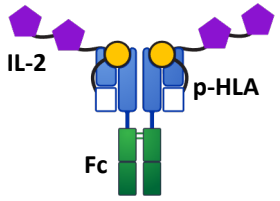
CUE-100 Series: Directing IL-2 Activity to Tumor-specific T cells and Avoiding Serious Off-target Side Effects

IL-2 Immuno-STAT

CUE-100 series



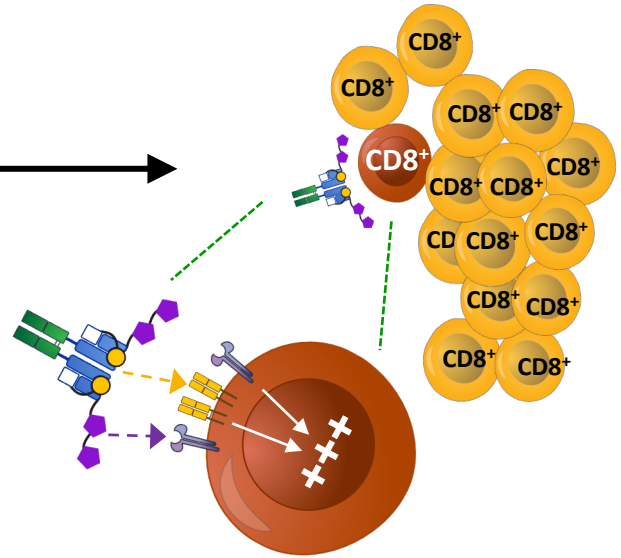
LEGEND

- IL-2
- IL-2R
- peptide-HLA
- TCR

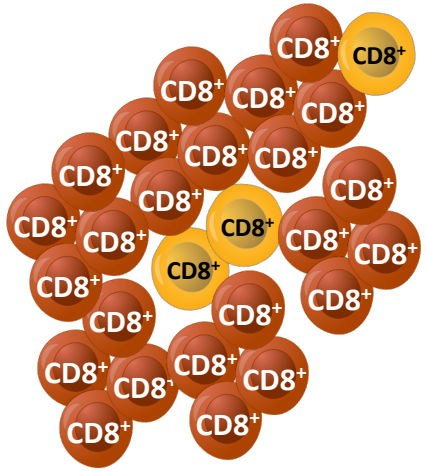
CD8+ TUMOR-SPECIFIC CD8+ T CELL

CD8+ NON TUMOR-SPECIFIC CD8+ T CELL

Focused Activity on Tumor-specific T cells



Biased Activation and Expansion of Tumor-specific T cells (or "TCR-engaged" T cells)



ADVANTAGES

- **Selective activity of IL-2 on tumor-specific T cells (cis-interaction)**
- **Potential for activation of TCR-engaged anti-tumor T cells (trans-interaction of IL-2)**
- **Demonstrated expansion of NK cells (*IL-2-mediated*)**
- **Minimize Treg activation**
- **Generally well-tolerated to date**
  lead candidate CUE-101 dosed up to 8.0 mg/kg with no MTD

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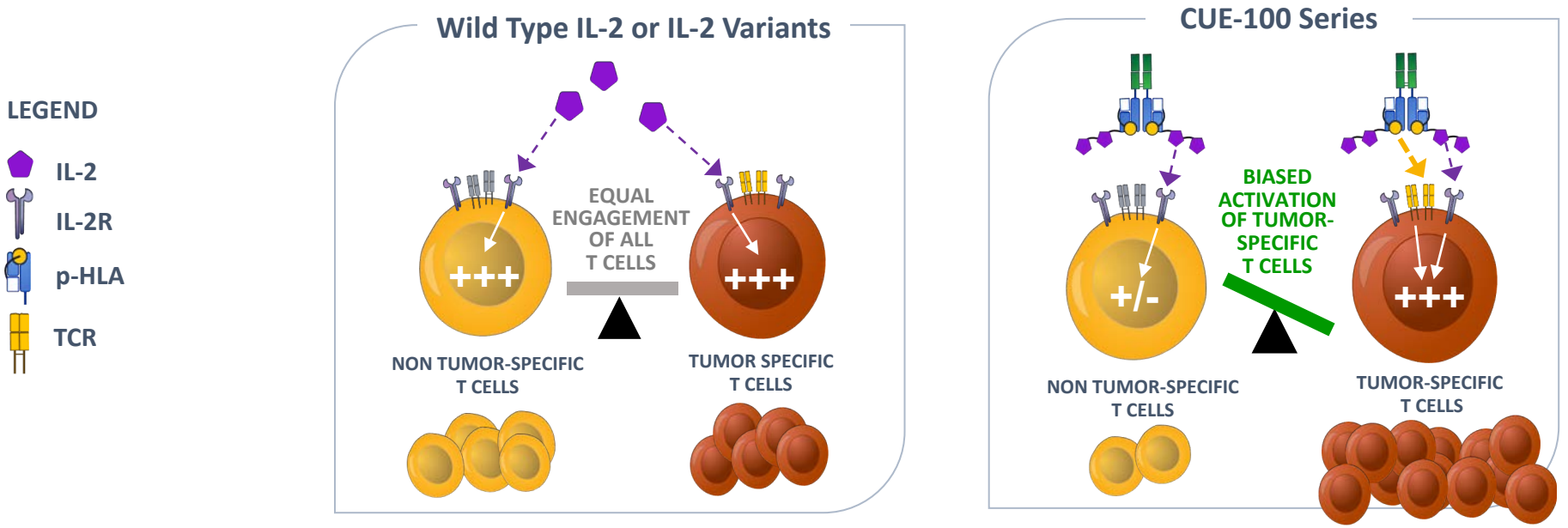
CUE-100 Series: Opportunity to Maximize the Fullest Potential of IL-2

IL-2-based CUE-100 series Immuno-STATs enable a larger therapeutic window for IL-2 effectiveness



TOLERATED CLINICAL DOSES	**0.037 mg/kg (approved dose)** **0.006 mg/kg (RP2D)** **0.006 to 0.024 mg/kg**	**Proleukin® (aldesleukin)** **Bempegaldesleukin (NKTR-214) and nemvaleukin alfa (ALKS-4230)** **SAR444245 (formerly THOR-707)**	**CUE-101 dosed up *to 8.0 mg/kg*** ***NO MTD identified***

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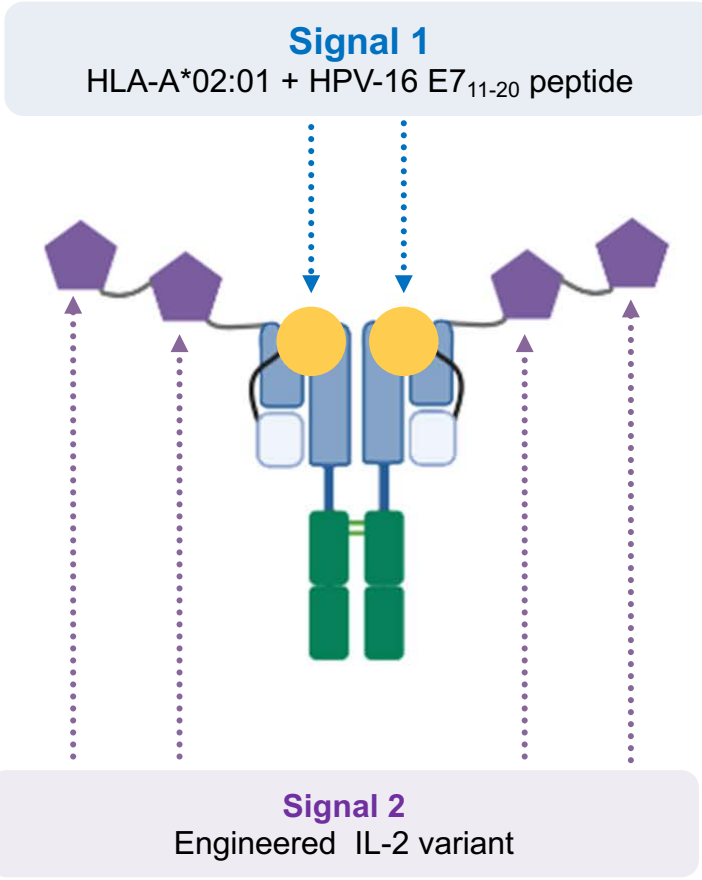
CUE-101: Lead Clinical Candidate Designed to Selectively Prime and Expand HPV E7-Specific T cells

CUE-101 Immuno-STAT Design



Clinical Rationale

- HPV is recognized as a growing driver of head and neck cancer in the US; despite treatment with current standards of care, >50% of patients with advanced disease will experience recurrence
- The HPV16 E7 protein is a primary driver of tumorigenesis and the E7 peptide presented by CUE-101 is a highly conserved T cell epitope and is immunogenic
- The CUE-101 clinical development strategy builds upon robust translational 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+

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CUE-101: Lead Clinical-stage Asset from IL-2 based CUE-100 Series

Overview of CUE-101 Phase 1 Monotherapy Part A Dose Escalation Study

Phase 1 Part A Dose Escalation Completed

- 38 patients with recurrent/metastatic H&N cancer across 7 dose escalation cohorts

PK

- Dose proportional exposure

PD

- Expansion of disease-relevant CD8+ T cells and NK cells, with evidence of tumor T cell infiltration

Tolerability

- Patients given CUE-101 doses ranging from 0.06 mg/kg – 8 mg/kg
- Generally well-tolerated with no MTD identified
- No evidence of anti-drug antibodies (ADAs) after repeated dosing

Efficacy

- Clinical activity observed across several dose cohorts (partial response/stable disease)
- PR observed in Cohort 6 dose (4.0mg/kg Q3W); selected as RP2D expansion cohort

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CUE-101 Phase 1 Part B Clinical Observations: RP2D 4 mg/kg
N = 10/12 Patients with Scans through C5

Clinical Responses	N	%
Objective Response *(CR or PR confirmed ≥ 4 weeks)*	1	10.0%
Durable Stable Disease *(SD sustained for ≥ 12 weeks*)*	3	30.0%
Clinical Benefit Rate *(CR/PR + durable SD)*	4	40.0%

**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

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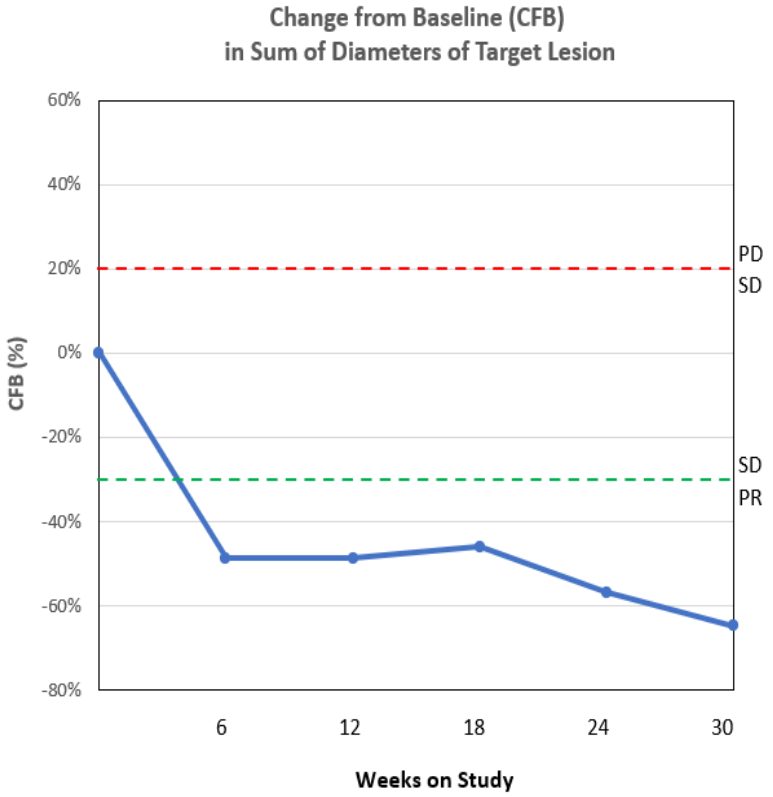
CUE-101: Confirmed PR with ~ 65% Reduction in Target Lesions

Case History

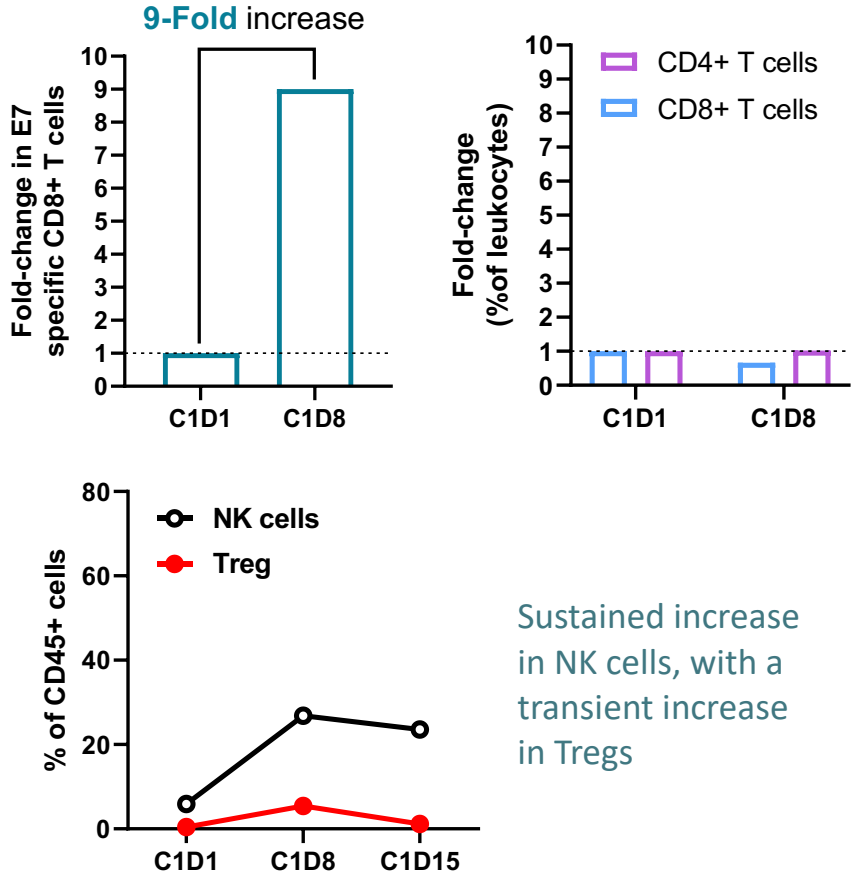
- Prior therapy:
  - 1L cetuximab
  - 2L pembrolizumab
- Progressive disease prior to enrollment
- Treated in metastatic 3L setting with 4.0 mg/kg CUE-101 Q3W (Cohort 6)
- Patient completed 10 cycles of CUE-101 and remains on study with PR ongoing



- Confirmed PR
- Duration of Response 24 weeks
- Patient remains on treatment

**Data updated 07SEP21*

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



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

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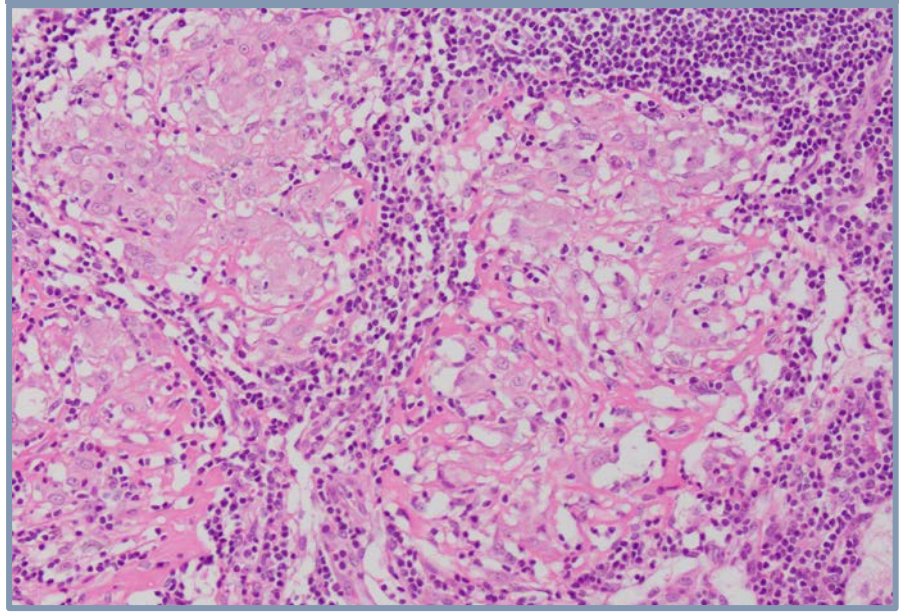
CUE-101: Tumor Necrosis and T Cell Infiltrates in Target Lesions

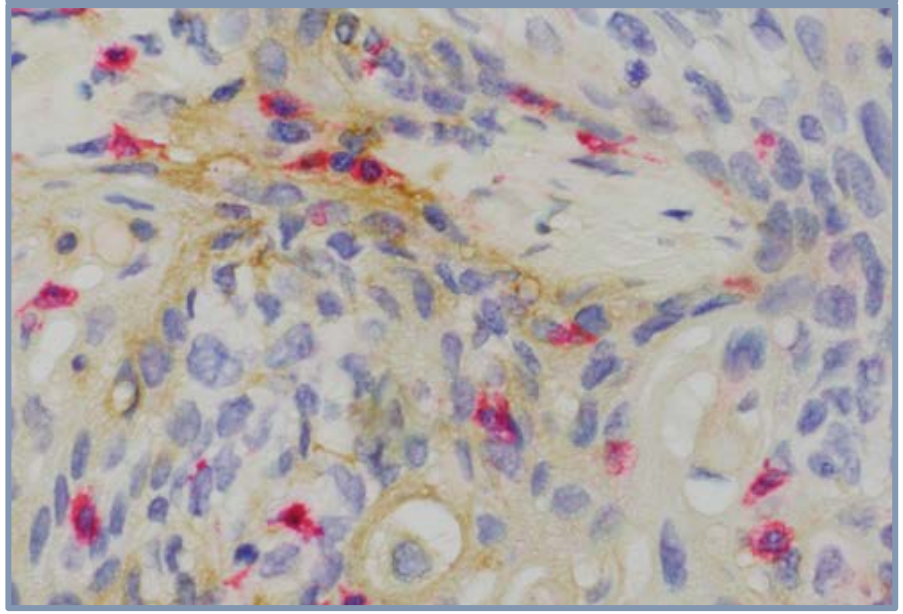
Case History

- Prior therapy:
  - 1L chemotherapy
  - 2L pembrolizumab
- Progressive disease prior to enrollment
- Treated in metastatic 3L setting with 1.0 mg/kg CUE-101 Q3W (Cohort 4)
- Confirmed and sustained SD through 18 weeks
- Target lesion resected at 18 weeks due to proximity to an artery

Hematoxylin and Eosin Stain



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



Patient remains disease free post resection

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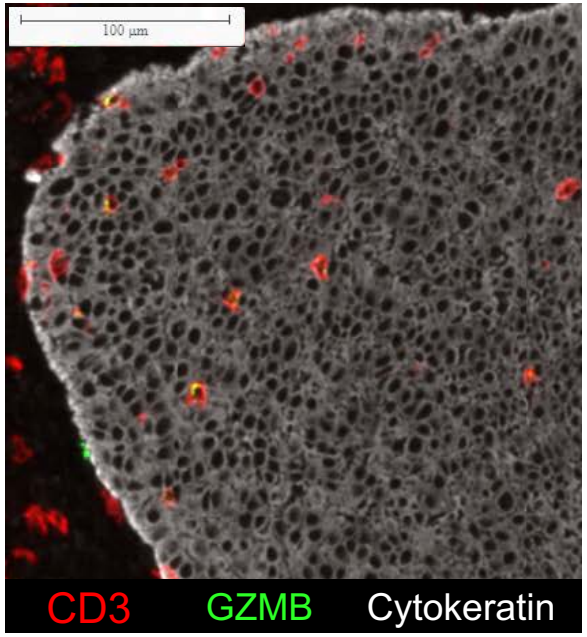
CUE-101: Increase in Tumor Infiltrating T Cells (TILs)

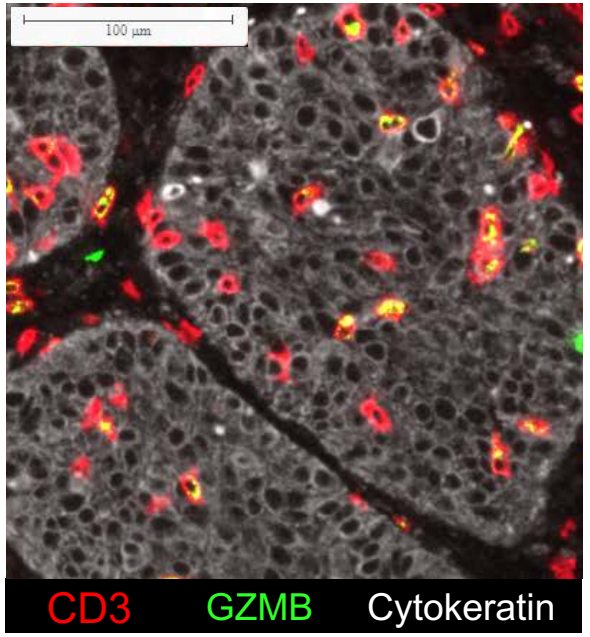
Case History

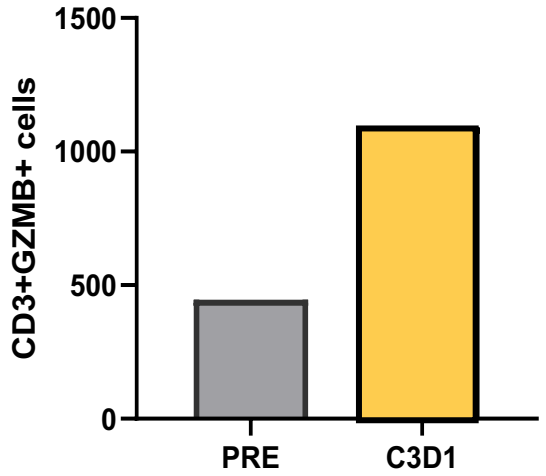
- Prior therapy:
  - 1L chemotherapy
  - 2L pembrolizumab
- Progressive disease prior to enrollment
- Treated in metastatic 3L setting with 2.0 mg/kg CUE-101 Q3W (Cohort 5)

Pre-dose



Cycle 3 Day 1





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

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CUE-101: Potential for Multiple Registration Paths

Monotherapy

- 2nd line+ therapy for HPV+ head and neck cancer

Combination therapy

- First line HPV+ Head and Neck cancer in combination with pembrolizumab

Neoadjuvant therapy

- Early treatment in neoadjuvant setting, neoadjuvant study launched in Q3 21, to demonstrate the value of CUE-101 treatment in patients prior to resection

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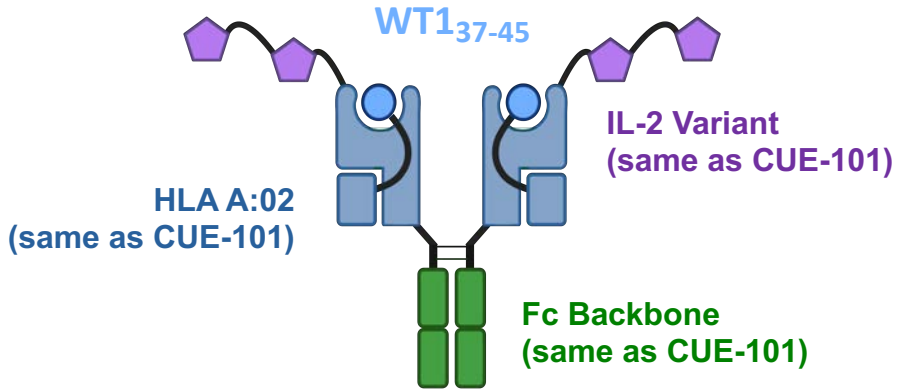
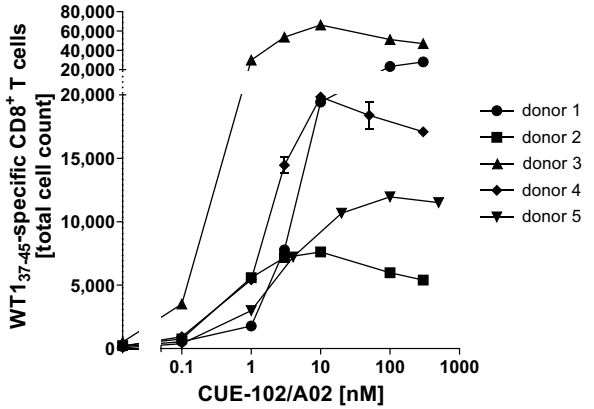
CUE-102: Wilms Tumor 1 (WT1) IND on Track for 1Q 2022 Filing

Molecular Design

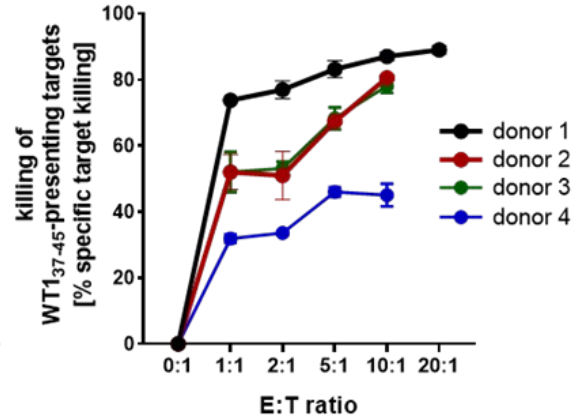


- Onco-fetal tumor antigen with restricted tissue-expression
- Top ranked cancer antigen by the National Cancer Institute (NCI)
- WT1 is expressed in over 20 types of hematological malignancies and solid tumors offering broad clinical opportunities

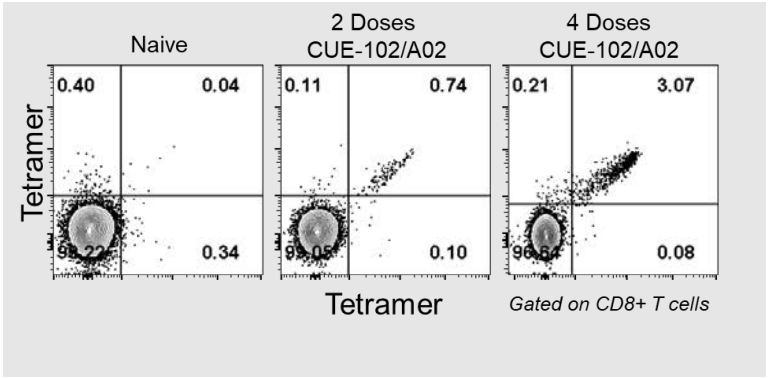
Human T cell expansion in vitro



WT-1 Target Killing



T cell priming and expansion in vivo in HLA-A02 transgenic mice



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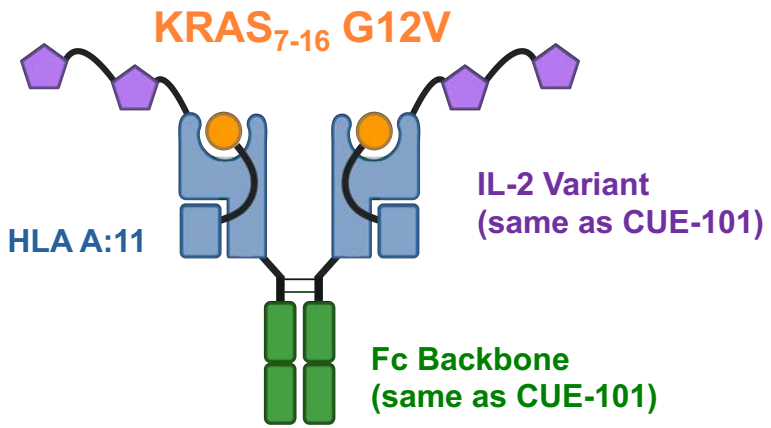
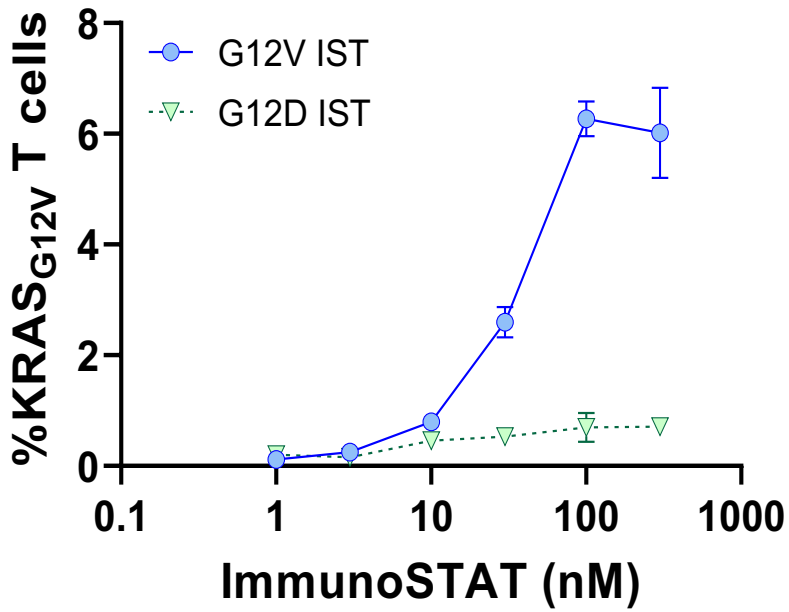
CUE-103: KRAS G12V Immuno-STAT

Molecular Design



- Builds on NCI (Rosenberg/Yang) studies that demonstrated clinical response using mutated KRAS-specific TILs/T cells
- KRAS G12V is a key driver mutation in highly prevalent solid tumors with significant remaining unmet need (NSCLC, CRC, PC, etc.);
- KRAS G12V A11 asset serves as a beachhead for other CUE-100 series molecules targeting KRAS mutations (i.e., G12D, G12R) and global alleles (i.e., A03, B07) - Source (UPenn PMID 34272369)

$KRAS_{G12V}$ T cell Expansion



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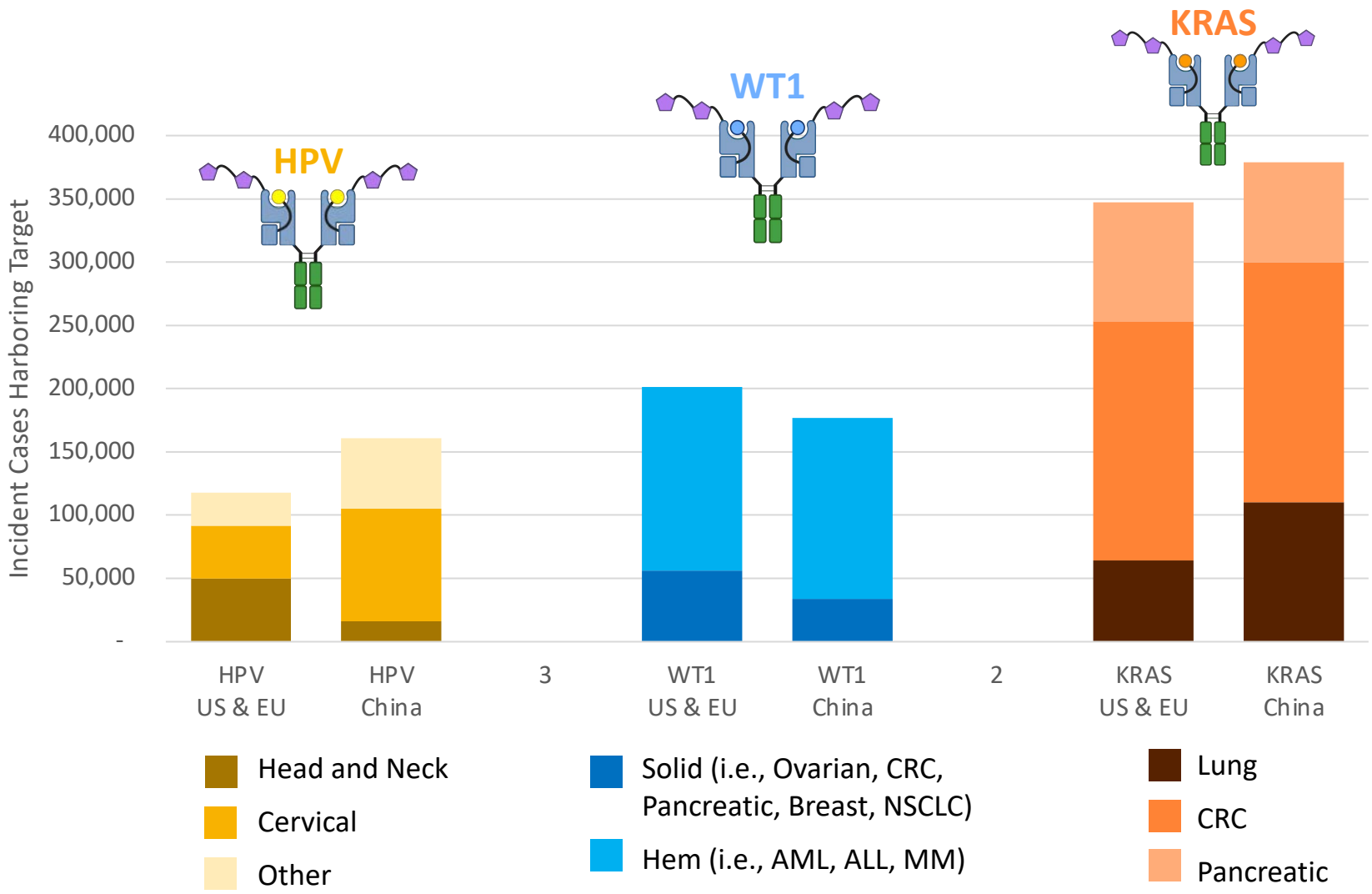
Expansion of Modular CUE-100 Series Into Broad Range of Cancers

Broad Universe of Addressable TCR Targets with CUE-100 Series

- Viral antigens (HPV, EBV)
- Cancer-Testes Antigens (WT1, MAGE)
- Lineage Antigens (Gp100)
- Neoantigens (KRAS)



Sources (Accessed 2020)
Annual Incidence: SEER (US), Globocan (EU and China)
Antigen Expression: NIH TGCA, Cancer Atlas

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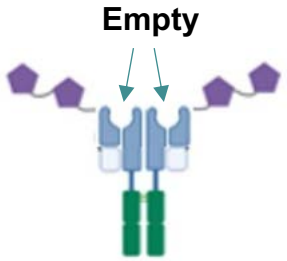
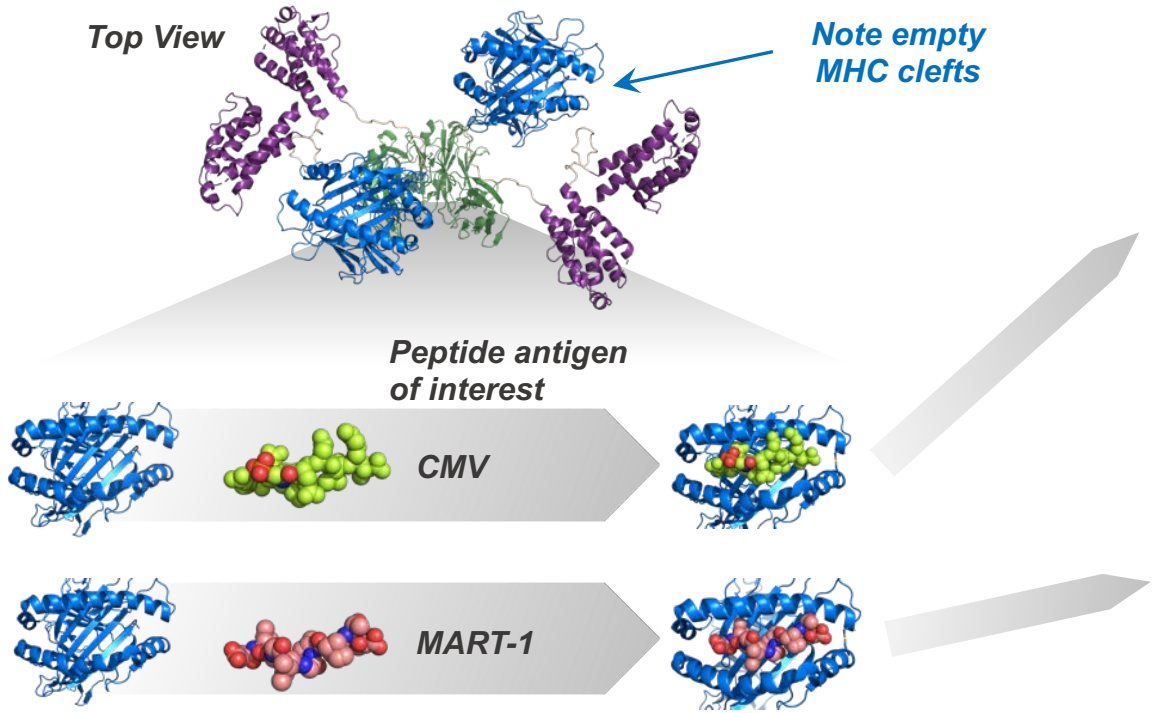
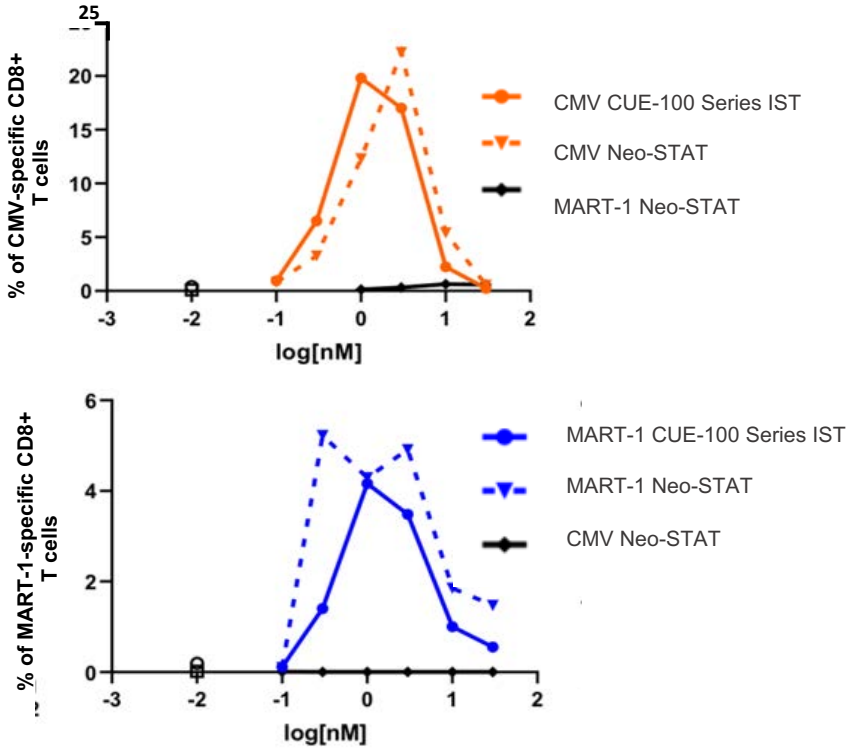
CUE-100 Neo-STAT: Universal Scaffold to Address Tumor Heterogeneity

Goal: To generate a universal immuno-STAT (IST) scaffold enabling more competitive development metrics *(time and cost efficiencies).*



Neo-STAT scaffold will be manufactured in bulk





Therapeutic Applications to include:

- Peptide mixes / Multi-antigen based cocktail therapy
- Integration of post-translationally modified peptides
- Extension to cancer neoantigens → Personalized medicine

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Summary of Strategic Developments for CUE 100 Series

CUE-101 monotherapy data

- Monotherapy holds promise of registration path for 3L+ HNSCC patients, and as a 2nd line therapy in CPS <1 patients who are not eligible for pembrolizumab
  - Clinical data de-risks CUE-101 as well as CUE-100 series
  - Demonstrates attractive PK/exposure and tolerability profile with evidence of clinical, anti-tumor activity
- Combination trial ongoing with pembrolizumab in 1L patients (potential for synergistic MoA)
- Neoadjuvant study launched Q3 (generate further evidence of TIL expansion and induction of tumor killing)

CUE-102 targets Wilms Tumor 1 (WT1) driven cancers – IND filing Q1 2022

- Broad opportunity across multiple solid and hematological cancers
- Preclinical data shows strong T cell expansion in response to CUE-102 from human PBMC

CUE-103 targeting KRAS G12V mutation – IND projected for 2023

- KRAS G12V is a key driver mutation in highly prevalent solid tumors
- CUE-103 serves as a beachhead for targeting other KRAS mutations and additional HLA alleles

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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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