Corporate Presentation

Immune Responses, On Cue™

Nasdaq: CUE

October 2020

Forward-Looking Statements

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Novel Platform to Harness the Power of the Immune System

Disruptive Platform for Disease-Relevant T Cell Modulation *In Vivo*

- The ***Immuno-STAT™*** *(**S**elective **T**argeting and **A**lteration of **T** cells) platform exploits the natural signals for T cell modulation.*
- *Off-the-shelf biologics with industry-standard manufacturing*
- *Administered directly into the patient with no need for ex-vivo manipulation*

Platform Modularity Enables Targeting Numerous Indications

- ***Immuno-STAT*** can incorporate diverse T cell epitopes and immuno-modulatory signals
- *Platform modularity can be deployed for many therapeutic areas including oncology, autoimmunity and infectious diseases*
- ***Neo-STAT*** *platform evolution enables enhanced productivity and scalability*

Focused Clinical Execution to De-Risk and Validate Platform

- ***CUE-101****, the lead clinical candidate, is in a multicenter monotherapy dose-escalation Phase 1 trial in HPV+ recurrent/metastatic (R/M) head and neck cancer*
- *Emerging results indicate dose-proportional exposure, favorable safety with signals of biologic and clinical activity*
- *Expansion of patient coverage via combo of CUE-101 with pembrolizumab in frontline R/M HNSCC*

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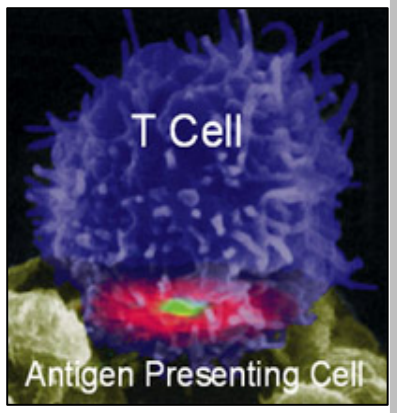
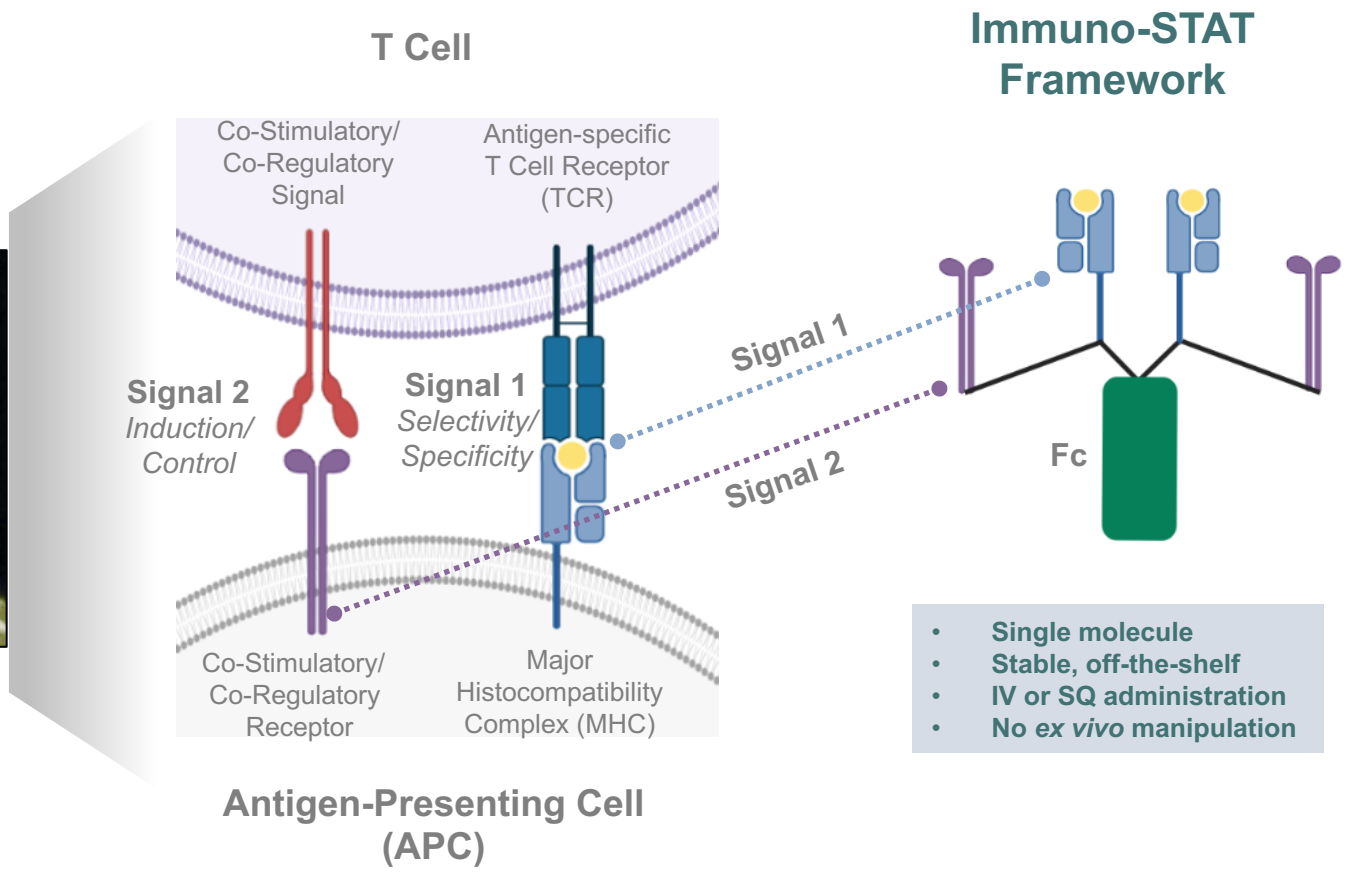
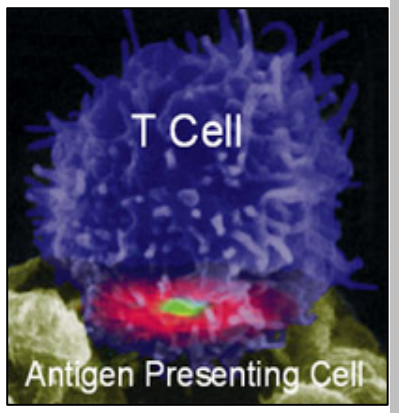
Emulating Nature's Cues to Selectively Modulate T Cells

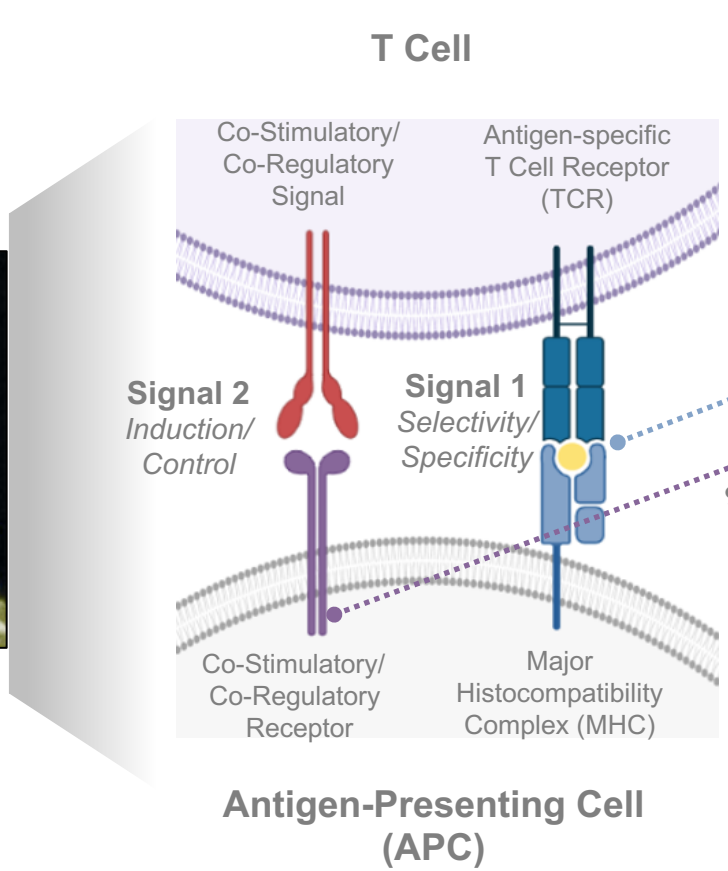


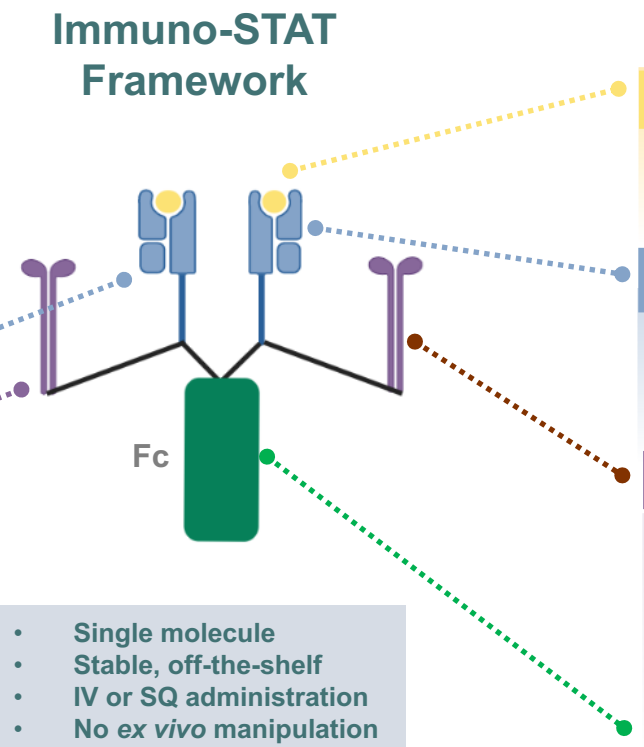


The Immuno-STAT platform can generate a wide diversity of therapeutic molecules for many diseases to selectively target and modulate the activity of disease-relevant T cells

Emulating Nature's Cues to Selectively Modulate T Cells







- **Single molecule**
- **Stable, off-the-shelf**
- **IV or SQ administration**
- **No *ex vivo* manipulation**

Platform Modularity

Peptide Antigen

Peptide epitopes to target different diseases

MHC

Different HLA alleles to address global patient populations

Co-stim/Co-reg

Distinct biological signals, including cytokines; cell-surface receptors; and/or other targeting modalities (e.g., scFv, etc.)

Fc Backbone

Fc engineering to dial in or out biological and effector functions

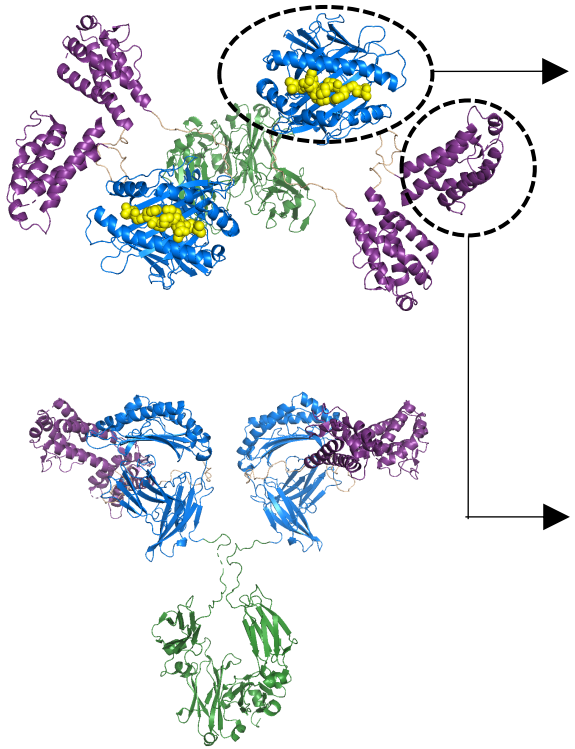
The Immuno-STAT platform can generate a wide diversity of therapeutic molecules for many diseases to selectively target and modulate the activity of disease-relevant T cells

CUE-100 Series: An Optimized Scaffold for Selective Delivery of Engineered IL-2 to Tumor-specific T cells

CUE-100 Series

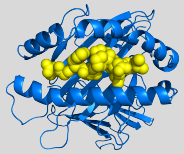
Top View

Side View



Immune Signaling Components

Tumor-Peptide Loaded HLA



"Signal 1" engagement of T cells via TCR:

- **Selective delivery of modified IL-2 to tumor-specific T cells**
- **Enables priming and expansion from naïve and pre-existing T cell repertoire**

Engineered IL-2

"Signal 2" engagement with engineered IL-2:

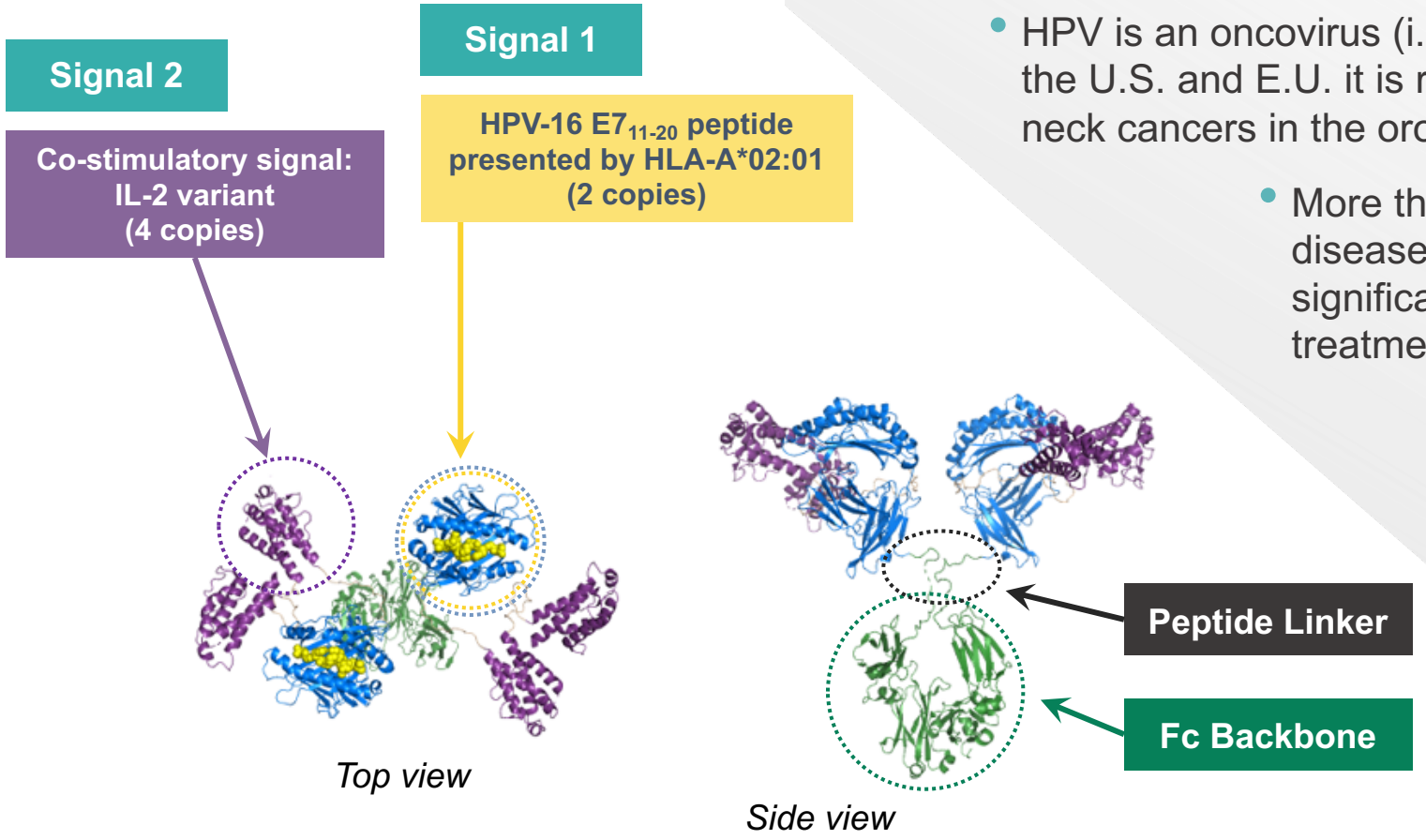
- **Abrogate binding to IL-2Rα: Minimize Treg activation**
- **Attenuate binding to IL-2Rβ: Allows for selective activation of tumor-specific T cells due to "signal-1" guided IL-2 (which minimizes activation of irrelevant T cells)**
- **CUE-100 series is "not alpha plus" thus differentiated mechanism of action over other "not-alpha" IL-2 variants**

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

CUE BIOPHARMA

CUE-101: Lead Clinical Candidate from CUE-100 Series

- CUE-101 is designed to selectively prime and expand HPV-specific T cells *in vivo*
  - HPV is an oncovirus (i.e., a virus that causes cancer) and in the U.S. and E.U. it is responsible for over 70% of head and neck cancers in the oropharyngeal region
    - More than 50% of patients with advanced disease will experience recurrence with significant quality of life impacts despite treatment with current standards of care
      - The CUE-101 clinical development strategy builds upon robust translational preclinical data and patient stratification

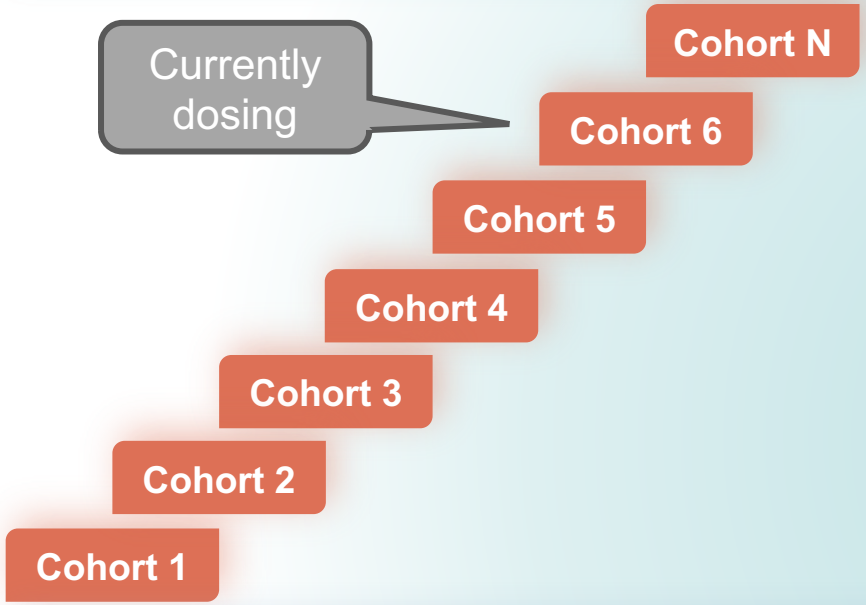


Platform Validation: Path from Concept to Clinical Application

- ☑ Deploy rational protein engineering to design core biologics scaffold for IL-2-based CUE-100 series
- ☑ CUE-101, lead clinical candidate from CUE-100 series, obtained IND approval in May 2019 for monotherapy in R/M HNSCC (2L+)
- ☑ CUE-101 demonstrates favorable safety profile (currently in Cohort 6 at 4 mg/kg)
- ☑ CUE-101 exhibits dose-proportional PK and exposure in patients
- ☑ CUE-101 demonstrates PD activity via expansion of tumor-specific T cells in early cohorts
- ☑ CUE-101 monotherapy Ph 1 dose escalation trial demonstrating signals of clinical activity
- ☑ 2ND trial of CUE-101 in combination with pembrolizumab (anti-PD-1) in frontline R/M HNSCC (Oct. 2020)

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

Part A: Monotherapy Dose Escalation



Part B: Monotherapy RP2D Expansion

Late Line Accelerated Monotherapy Approval Opportunity in Head and Neck Cancer

- **Eligibility (Part A and B)**
  - HPV-16+ Head and Neck Cancer
  - Recurrent/Metastatic (R/M)
  - Second Line or Greater (2L+)
- **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 Dosing)
  - HPV E7-specific CD8+ T cell counts
  - HPV E7-specific CD8+ T cell functionality
  - Immunophenotyping, cytokine release, and T cell receptor (TCR) sequencing
- **NCT03978689**

(PD, pharmacodynamics; PK, pharmacokinetics; RP2D, Recommended Phase 2 Dose)

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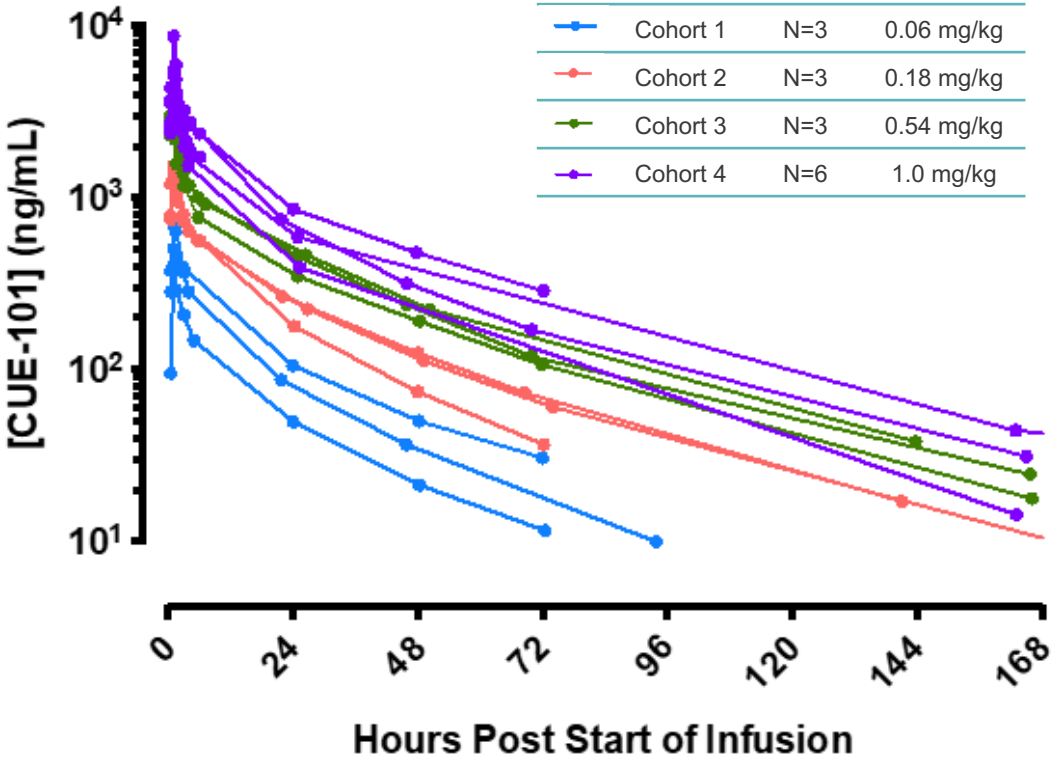
CUE-101: Part A Dose Cohorts

Cohort	CUE-101 Dose (mg/kg)	CUE-101 IL-2 Molar Content Relative to Approved Proleukin Dose
Cohort 1 ✓	0.06	~ 0.46x
Cohort 2 ✓	0.18	~ 1.4x
Cohort 3 ✓	0.54	~ 4.3x
Cohort 4 ✓	1.0	~ 8.0x
Cohort 5 ✓	2.0	~ 16.0x
Cohort 6 ✓	4.0	~ 32.0x
Cohort 7	8.0	~ 64.0x

Average prior lines of therapy: ~4; Range: 2-6
Average number of prior drugs: ~5; Range: 2-9

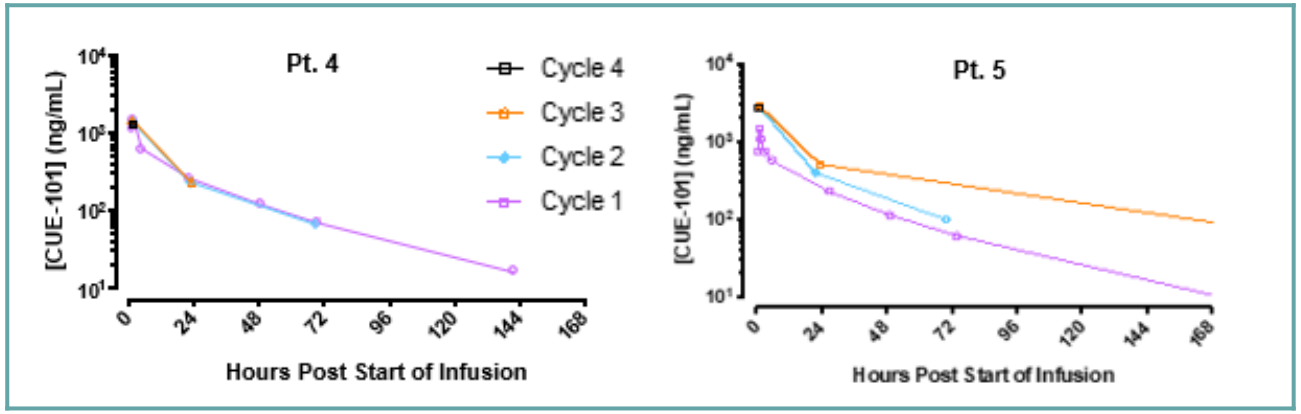
CUE-101 PK and PD: Dose-Proportional & Repeat Exposures from Cohorts 1 – 4, and Evidence of PD Activity



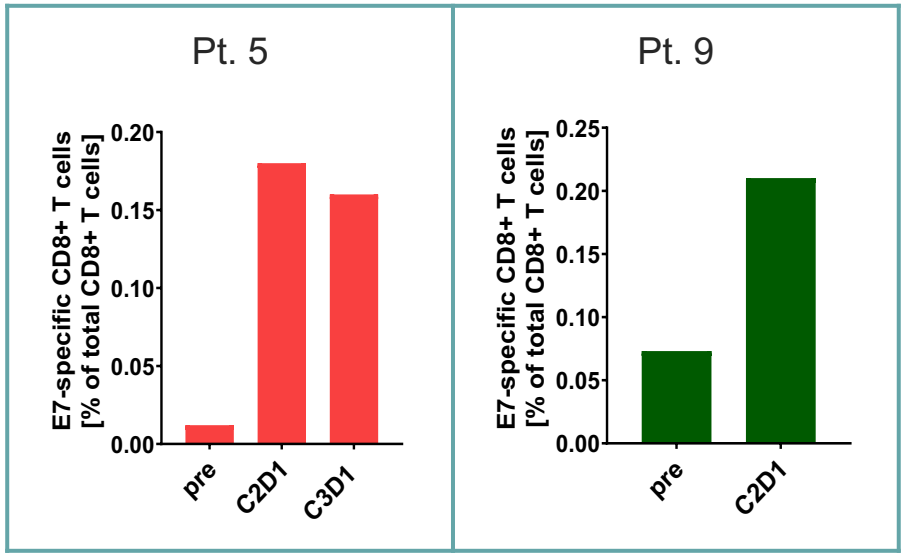
CUE-101 PK and PD update:

- Increase in dose-dependent exposure supports continued dose escalation
- Exposures are broadly in line with pre-clinical projections
- Repeated dosing in the same patient demonstrates comparable exposure
- Early evidence of PD activity via HPV-specific T cell expansion

Examples of comparable exposure upon repeated dosing

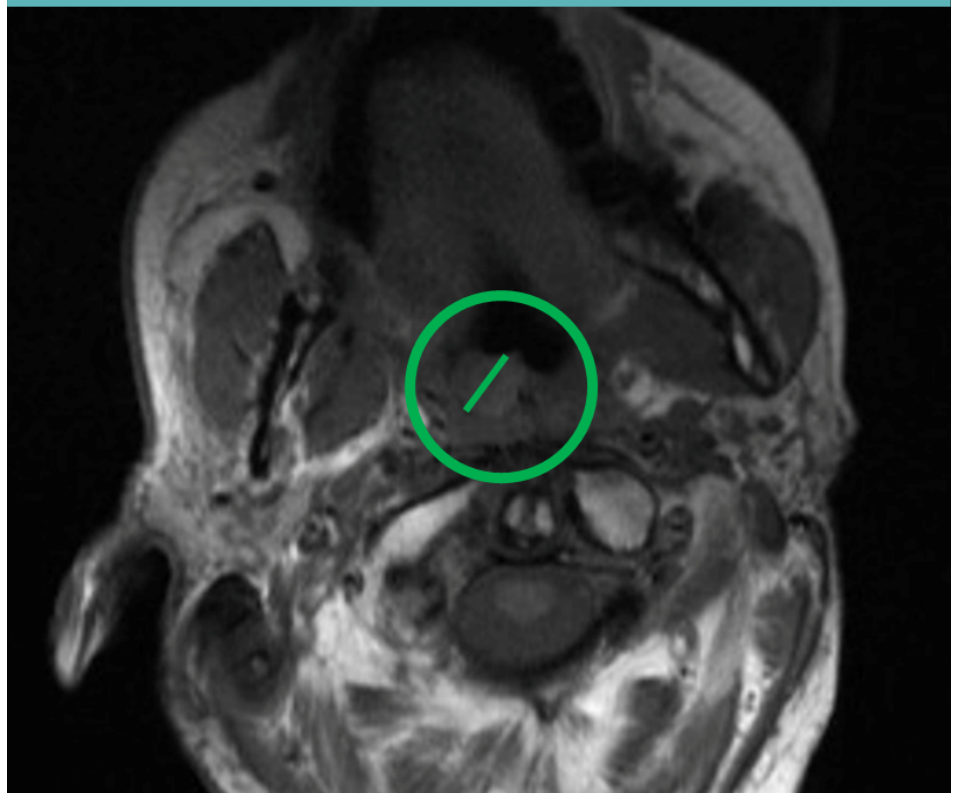


Examples of T cell expansion post-dosing



CUE-101: Cohort 2 Patient #6 Case Study

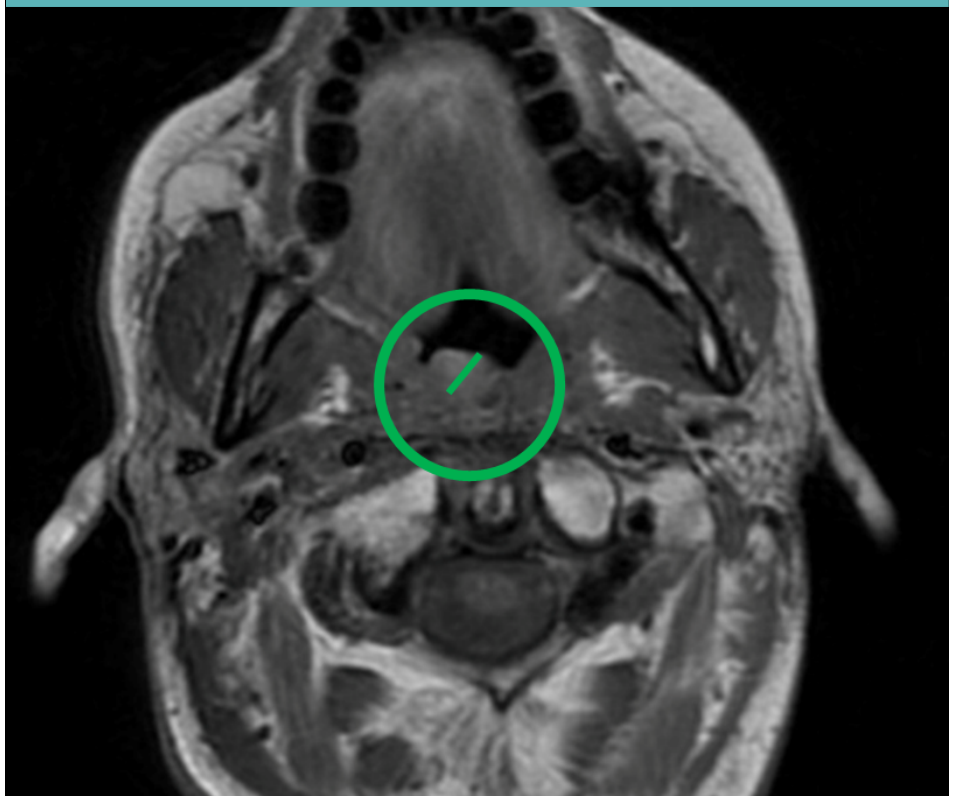
Day 0: Baseline Tumor



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

Patient received multiple prior lines of therapy, including checkpoint inhibition

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

CUE BIOPHARMA

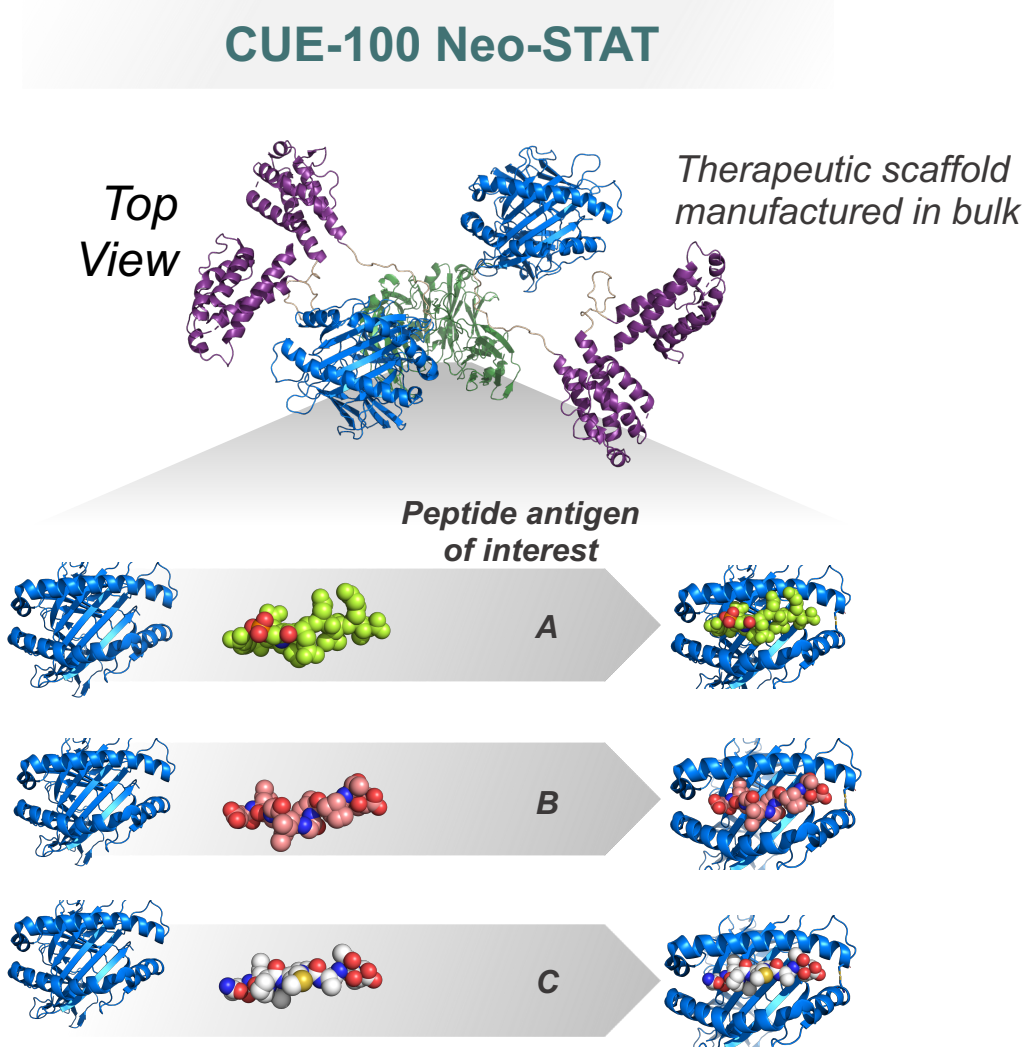
CUE-101: Phase I Clinical Development Network

- **Emory Winship Cancer Institute**: Nabil Saba
- **Karmanos Cancer Institute**: Elizabeth Heath and Ammar Sukari
- **MD Anderson Cancer Center**: Bonnie Glisson
- **Memorial Sloan Kettering Cancer Center**: Lara Dunn
- **MGH/Harvard and Dana Farber Cancer Institute**: Sara Pai and Lori Wirth
- **Moffitt Cancer Center**: Christine Chung
- **Sidney Kimmel Comprehensive Cancer Center-Johns Hopkins**: Tanguy Seiwert
- **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 14 Phase I sites are now open

CUE™ BIOPHARMA

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

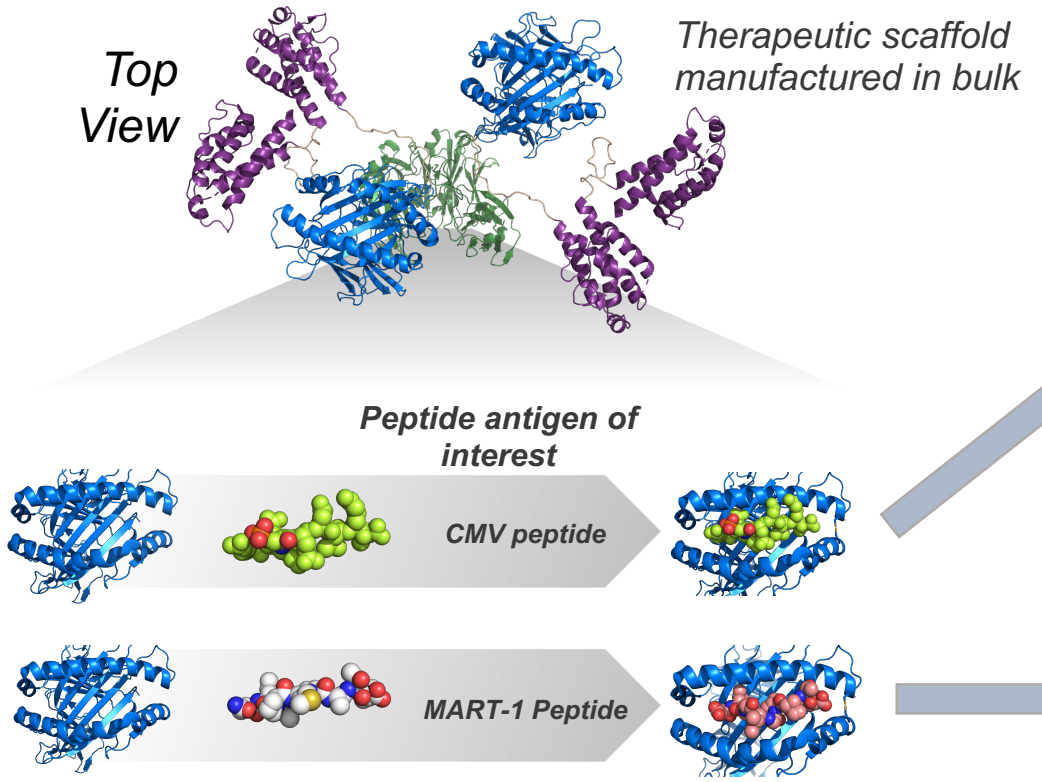


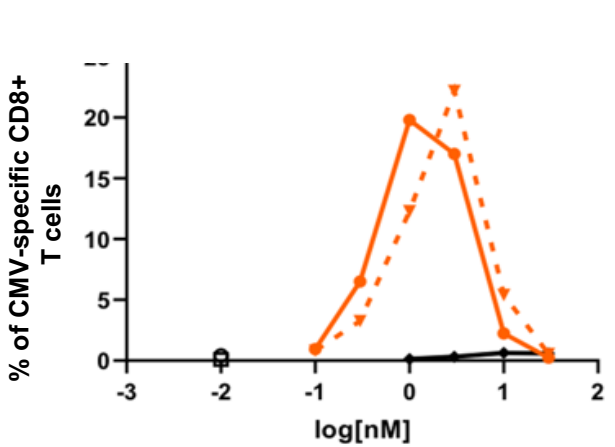
Therapeutic scaffold receptive for chemical conjugation of peptides that potentially:

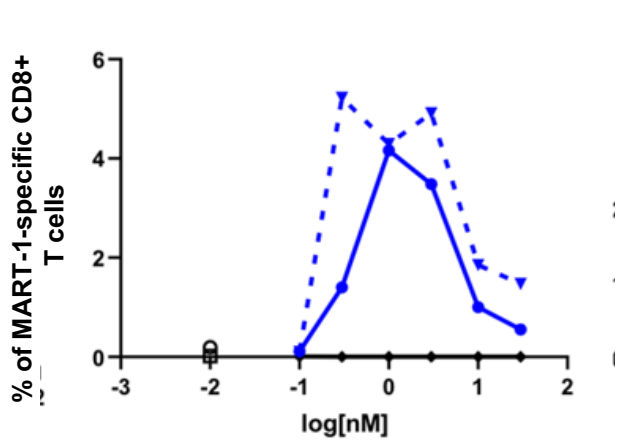
- **Increases R&D efficiency** and reduces cost of the generation of clinical grade material on the CUE-100 framework
- **Enables targeting of multiple tumor antigens** including post-translationally modified peptides and neo-antigens for personalized therapy
- **Applications in infectious diseases** for induction of robust anti-pathogen T cell responses

Neo-STAT: PoC with Viral and Tumor T Cell Antigens

CUE-100 Neo-STAT

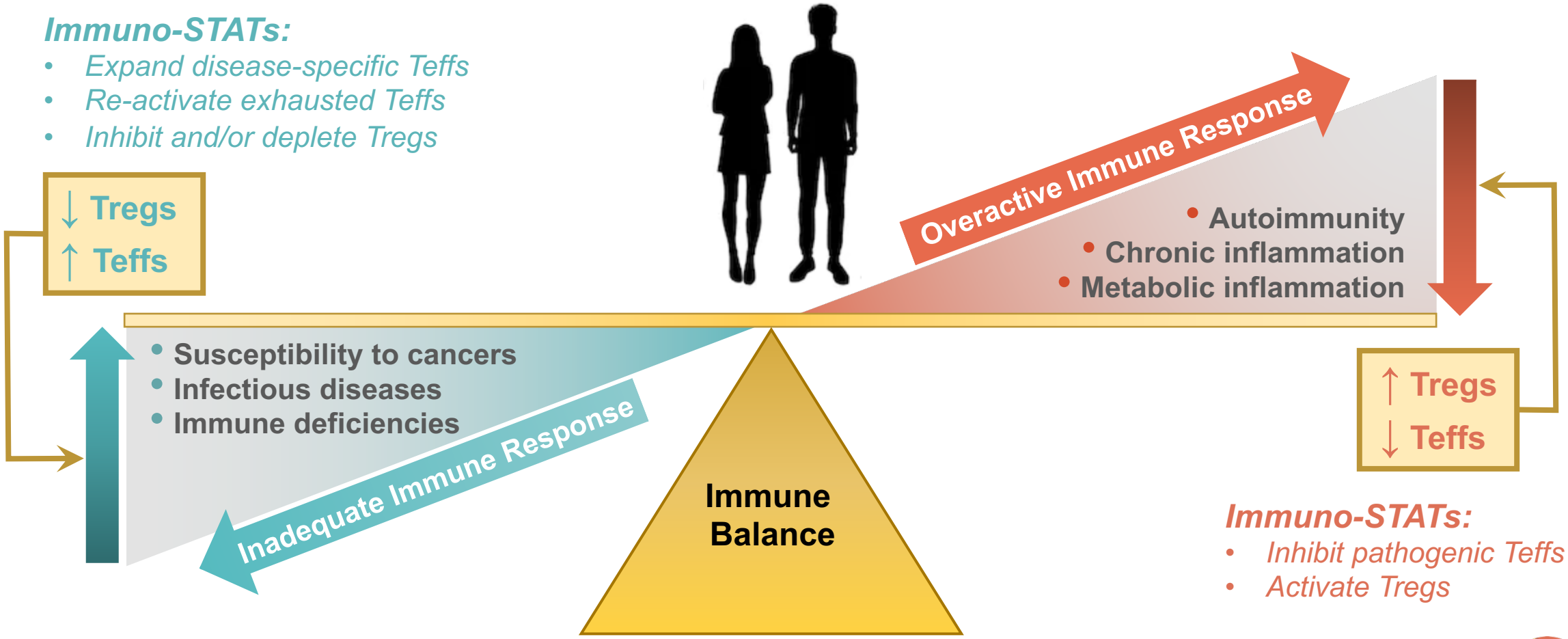






Immuno-STATs and Neo-STATs are Designed to Restore Immune Balance

Immuno-STATs:
- *Expand disease-specific Teffs*
- *Re-activate exhausted Teffs*
- *Inhibit and/or deplete Tregs*

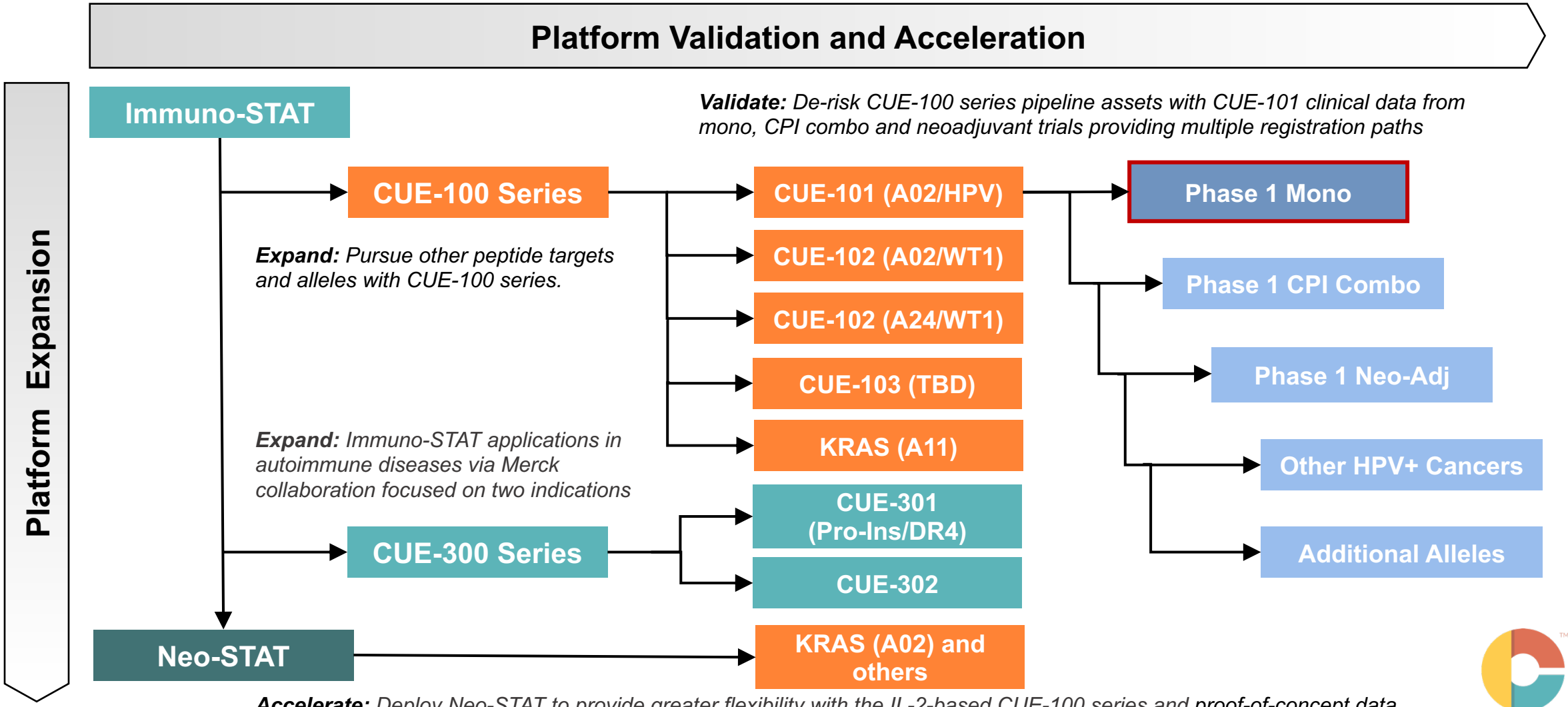


Immuno-STATs:
- *Inhibit pathogenic Teffs*
- *Activate Tregs*

Restoration of immune balance is a key pillar of human health

Key: Teffs, effector T cells; Tregs, regulatory T cells

Corporate Development and Growth Strategy



Recent Publications Underscore Potential Mechanistic Advantages

Demonstrates that the core scaffold of the Immuno-STAT can penetrate solid tumors and directly engage TILs

nature methods

ARTICLES

https://doi.org/10.1038/s41592-020-0934-5

In vivo detection of antigen-specific CD8+ T cells by immuno-positron emission tomography

Andrew W. Woodham[1,2,10], Stad H. Zeigler[3,10], Ella L. Zeyang[4,10], Stephen C. Kolifrath[1,2], Ross W. Cheloha[1,2], Mohammad Rashidian[5], Rodolfo J. Chaparro[6], Ronald D. Seidel[6], Scott J. Garforth[3], Jason L. Dearling[7], Maia Mesyngier[1,4], Phaneendra K. Duddempudi[3], Alan B. Packard[8], Steven C. Almo[9] ✉ and Hidde L. Ploegh[1,2] ✉

Sept. 2020

CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

CUE-101, a Novel E7-pHLA-IL2-Fc Fusion Protein, Enhances Tumor Antigen-Specific T-Cell Activation for the Treatment of HPV16-Driven Malignancies

Steven N. Quayle[1], Natasha Girgis[1], Dharma R. Thapa[1], Zohra Merazga[1], Melissa M. Kemp[1], Alex Histed[1], Fan Zhao[1], Miguel Moreta[1], Paige Ruthardt[1], Sandrine Hulot[1], Alyssa Nelson[1], Lauren D. Kraemer[1], Dominic R. Beal[1], Luke Witt[1], Jessica Ryabin[1], Jonathan Soriano[1], Mark Haydock[1], Emily Spaulding[1], John F. Ross[1], Peter A. Kiener[2], Steven Almo[3], Rodolfo Chaparro[1], Ronald Seidel[1], Anish Suri[1], Saso Cemerski[1], Kenneth J. Pienta[4], and Mary Ellen Simcox[1]

[1]Cue Biopharma, Cambridge, Massachusetts. [2]BioKien LLC, Potomac, Maryland. [3]Departments of Biochemistry and Physiology and Biophysics, Albert Einstein College of Medicine, Bronx, New York. [4]The Brady Urological Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland.

April 2020

PLOS ONE

RESEARCH ARTICLE

Mechanistic dissection of the PD-L1:B7-1 co-inhibitory immune complex

Sarah C. Garrett-Thomson[1]*, Aldo Massimi[1], Elena V. Fedorov[1], Jeffrey B. Bonanno[1], Lisa Scandiuzzi[2], Brandan Hillerich[3], Ronald D. Seidel, III[3], James D. Love[1], Scott J. Garforth[1], Chandan Guha[2], Steven C. Almo[1]*

1 Department of Biochemistry, Albert Einstein College of Medicine, Bronx, New York, United States of America, **2** Department of Radiation Oncology, Albert Einstein College of Medicine, Bronx, New York, United States of America, **3** Cue BioPharma Inc., Cambridge, Massachusetts, United States of America

June 2020

CUE BIOPHARMA

Corporate Accomplishments and 2020 Guidance

Key Accomplishments

- Ongoing timely enrollment through Cohorts 1-5 in our dose-escalation Phase 1 CUE-101 monotherapy trial
- Safety clearance to initiate enrollment of Cohort 6
- To date, CUE-101 has been very well tolerated
- Dose-proportional exposure demonstrated
- Evidence of PD activity and signs of potential monotherapy clinical activity
- Generated pilot data with CUE-102 targeting WT-1 demonstrating *ex vivo* T cell expansion
- Demonstrated preclinical proof of concept of our Neo-STAT platform

2020 Guidance

In 2H20:

- Evaluate clinical responses in Phase I CUE-101 via RECIST criteria
- Initiate combination trial with Keytruda in frontline HPV+ head and neck squamous cell carcinoma
- Initiate and extend IND-enabling activities for CUE-102
- Select target for CUE-103
- Demonstrate Neo-STAT platform manufacturability and efficiencies
- Identify potential clinical candidates for the treatment of autoimmune diseases

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

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Thank you

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