Corporate Presentation

Immune Responses, On Cue™

Nasdaq: CUE | March 2020

Cowen & Co. 40th Annual Healthcare Conference | March 2, 2020

Forward-Looking Statements

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This presentation contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that are intended to be covered by the “safe harbor” created by those sections. Forward-looking statements, which are based on certain assumptions and describe our future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such as “believe,” “expect,” “may,” “will,” “should,” “would,” “could,” “seek,” “intend,” “plan,” “goal,” “project,” “estimate,” “anticipate,” “strategy,” “future,” “likely” or other comparable terms. All statements other than statements of historical facts included in this press release regarding our strategies, prospects, financial condition, operations, costs, plans and objectives are forward-looking statements. Examples of forward-looking statements include, among others, statements we make regarding anticipated results of our drug development efforts, including study results, our expectations regarding the timing of milestone events, regulatory developments and expected future operating results. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, our limited operating history, limited cash and a history of losses; our ability to achieve profitability; our ability to secure required U.S. Food and Drug Administration (“FDA”) or other governmental approvals for our product candidates and the breadth of any approved indication; negative or inconclusive results from our clinical studies or serious and unexpected drug-related side effects or other safety issues experienced by participants in our clinical trials; delays and changes in regulatory requirements, policy and guidelines including potential delays in submitting required regulatory applications to the FDA; our reliance on licensors, collaborations and strategic alliances; our ability to obtain adequate financing to fund our business operations in the future; and the other risks and uncertainties described in the Risk Factors and in Management's Discussion and Analysis of Financial Condition and Results of Operations sections of our most recently filed Annual Report on Form 10-K and any subsequently filed Quarterly Report(s) on Form 10-Q. Any forward-looking statement made by us in this presentation is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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BIOPHARMA

Corporate Highlights

Disruptive Platform for T Cell Modulation *In Vivo*

- 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 with initial data in 1H 2020
- Platform modularity demonstrated through CUE-102 for WT1-associated cancers
- Neo-STAT capability enhances R&D efficiency and offers potential for personalized immunotherapy

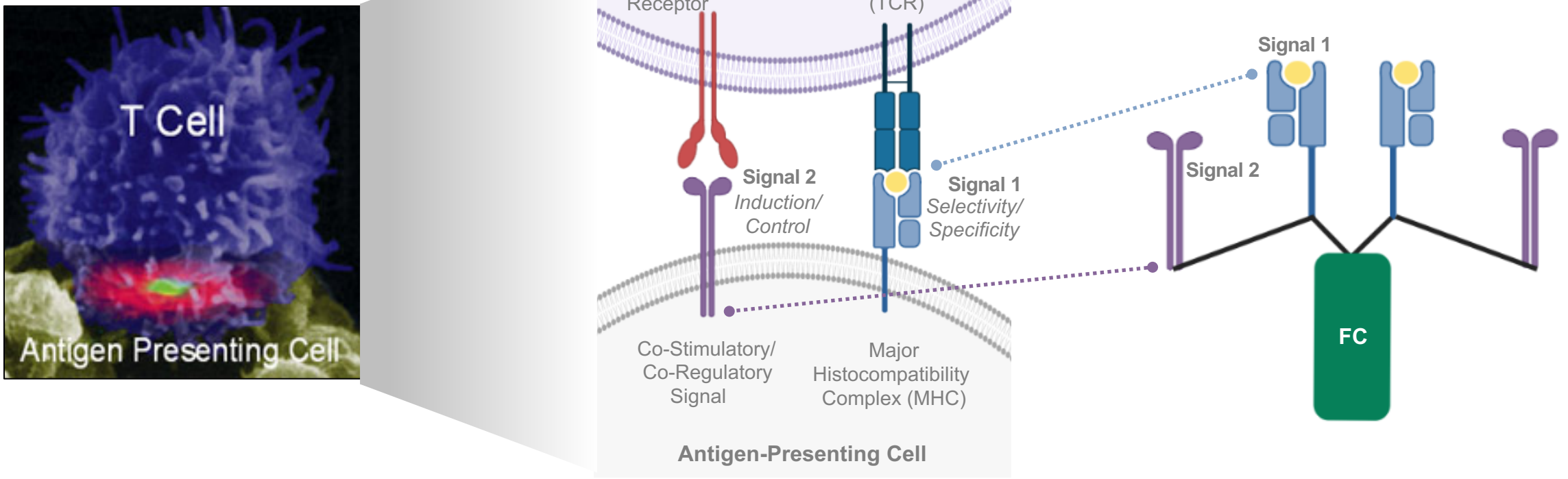
Strategic Partnerships to Accelerate Expansion

- LG Chem collaboration to expand IL-2 based CUE-100 series in immuno-oncology
- Merck collaboration to establish proof of mechanism for Immuno-STAT platform in autoimmune disease

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

CUE™ BIOPHARMA

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

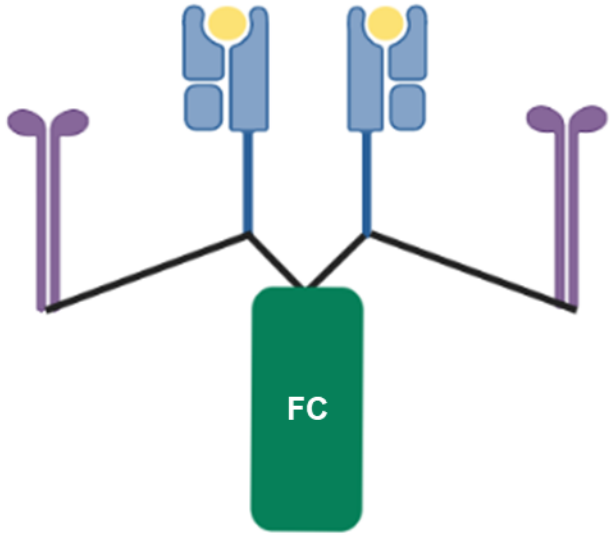
Immuno-STAT Modularity

Peptide

Peptide epitopes to target different diseases

MHC

Different HLA alleles to address global patient populations



Co-stim/Co-reg

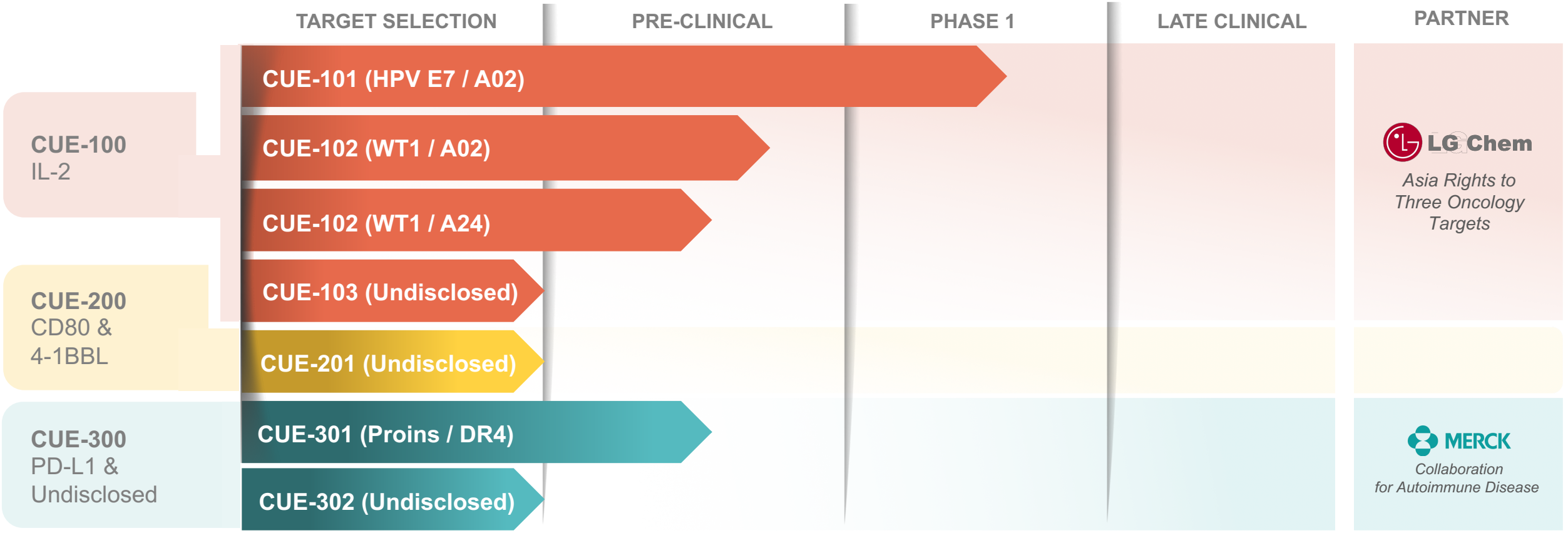
Distinct biological signals, including cytokines; cell-surface receptors; and/or other targeting modalities (e.g., scFv, etc.)

Fc Backbone

Fc engineering to dial in or out biological and effector functions

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

Pipeline

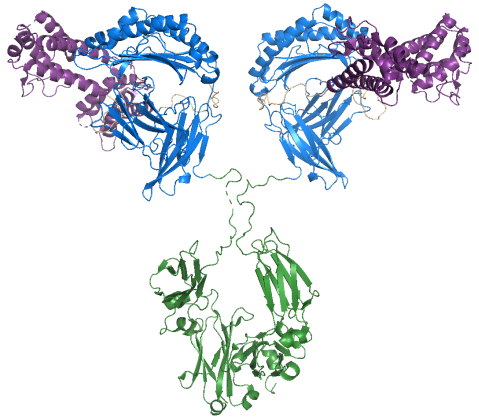


CUE BIOPHARMA

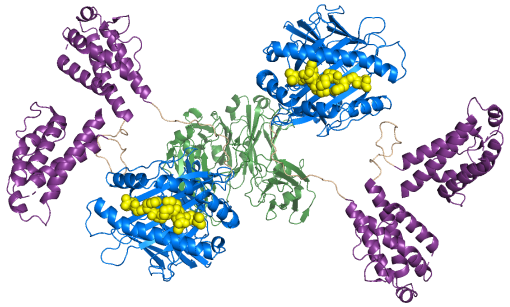
CUE-100 Series: Exploiting IL-2 via Rational Protein Design

CUE-100 Series

Side View

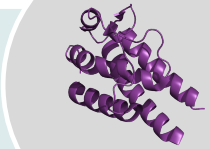


Top View



Immune Signaling Components

Attenuated IL-2

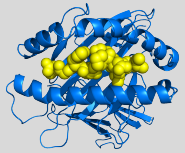


Optimized for desired biological activity through two single amino acid changes

- Abrogates binding to IL-2R alpha
- Reduces binding affinity to IL-2R beta

Maintains IL-2 ability to stimulate antigen-specific CD8+ T cells while reducing Treg expansion

Peptide Loaded HLA



Stabilized peptide HLA complex to present disease-relevant epitope to T cell receptor

- Framework allows for incorporation of an array of HLA Class I alleles (i.e., A02, A11, A24)

Provides "Signal 1" to the targeted antigen-specific CD8+ T cells, thereby enhancing the activity of the attenuated IL-2

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

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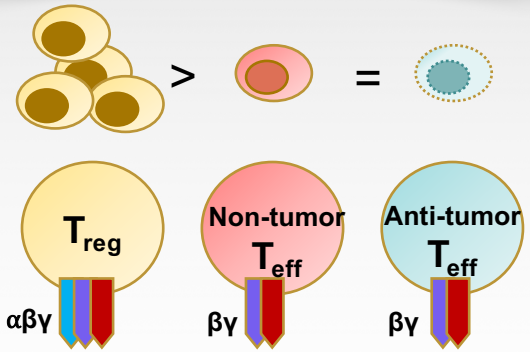
CUE-100 Series: Mechanistic Differentiation Over Emerging "Not Alpha" IL-2 Landscape

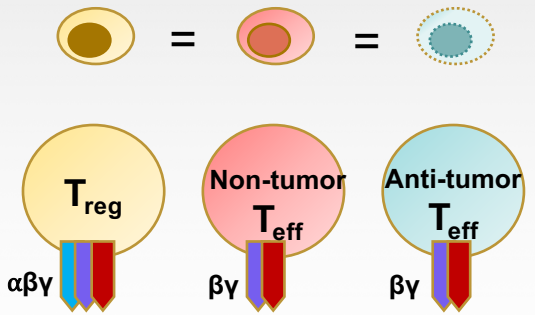
IL-2Rα
IL-2Rβ
IL-2Rγ

Wild Type IL-2 *(e.g., Proleukin)*



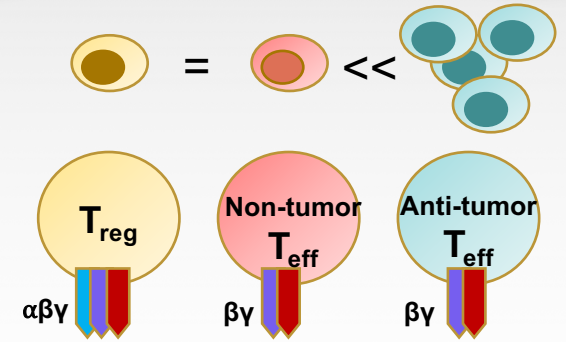
- Expansion of Tregs
- Expansion of non-tumor Teffs
- Expansion of tumor-specific T cells, if pre-existing

"Not Alpha" IL-2 *(e.g., THOR-707)*



- **Reduced expansion of Tregs**
- Expansion of non-tumor Teffs
- Expansion of tumor-specific T cells, if pre-existing

CUE-100 IL-2 Series *(e.g., CUE-101)*

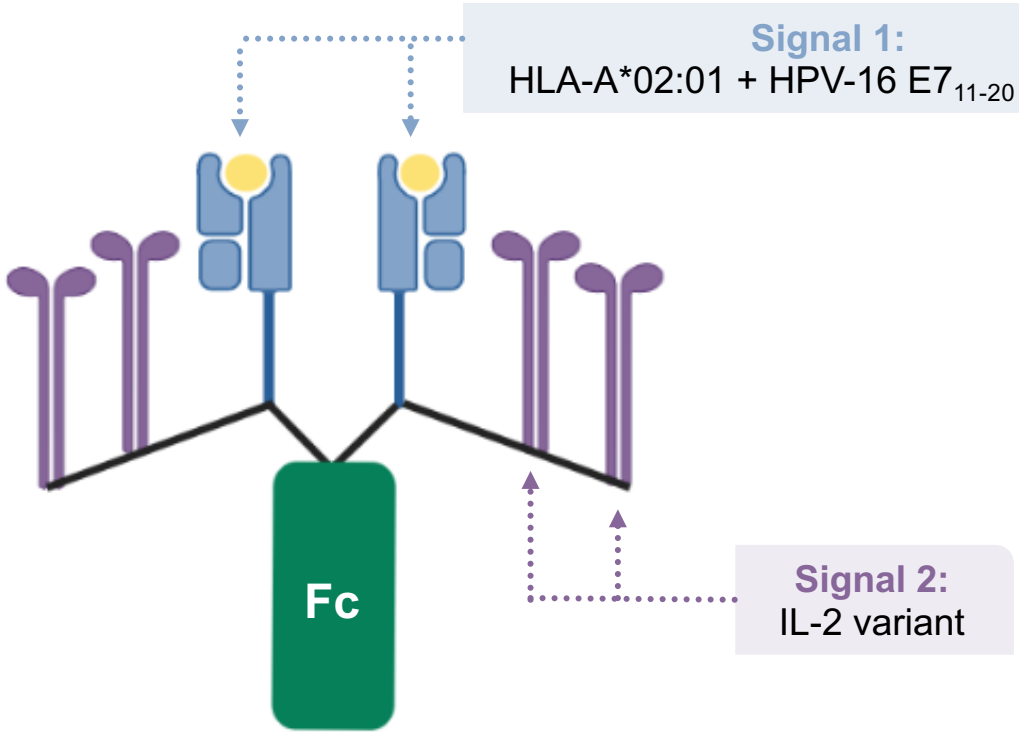


- **Reduced expansion of Tregs**
- **Reduced expansion of non-tumor Teffs**
- **Expansion of pre-existing tumor-specific T cells and priming of naïve T cells**

CUE-100 series is designed for selective induction and expansion of tumor-specific CD8+s without reliance on a pre-existing repertoire

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

CUE-101 Immuno-STAT Design

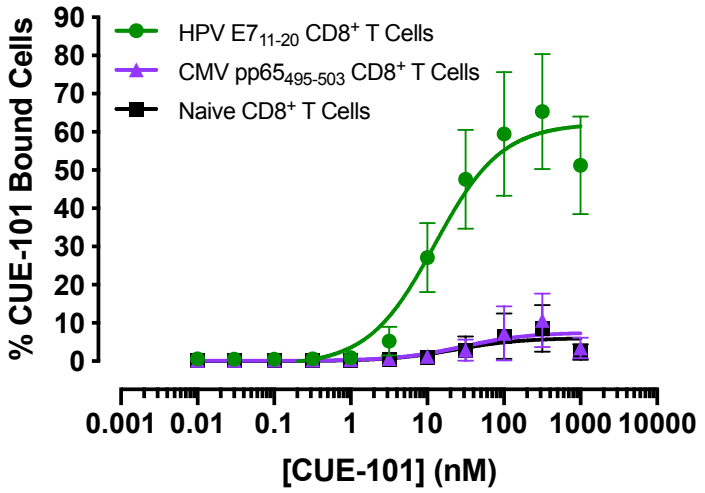


Clinical Rationale

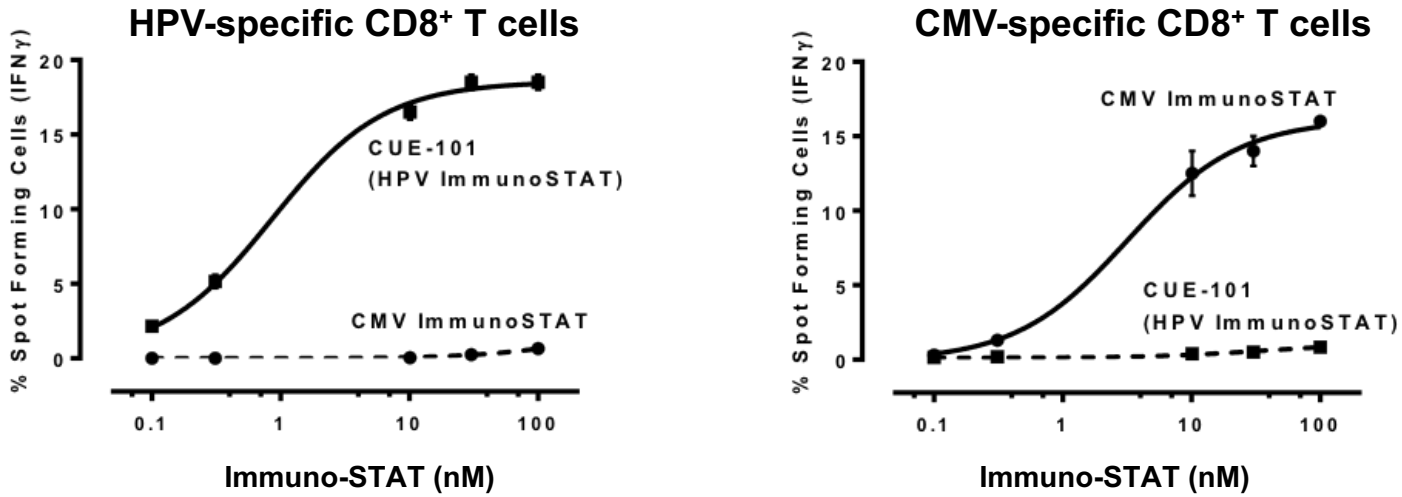
- CUE-101 is designed to selectively prime and expand HPV-specific T cells in vivo
- HPV is recognized as a growing driver of head and neck cancer and is now responsible for over 70% of oropharyngeal cancers in the US and EU
- Despite treatment with current standards of care, more than 50% of patients 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: Directing IL-2 to the "Right" T Cells

Selective Binding

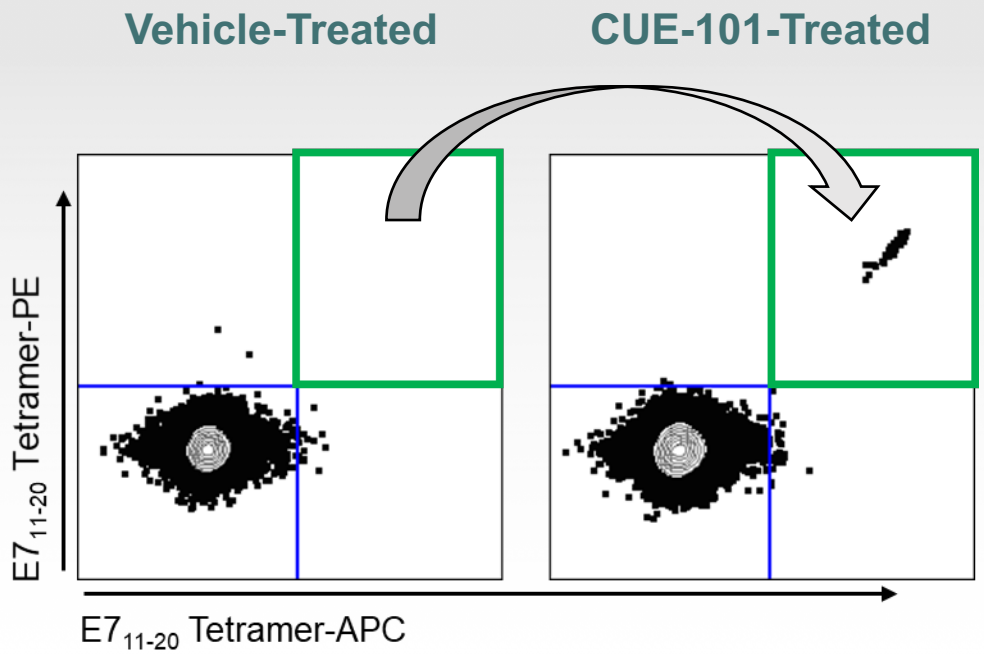


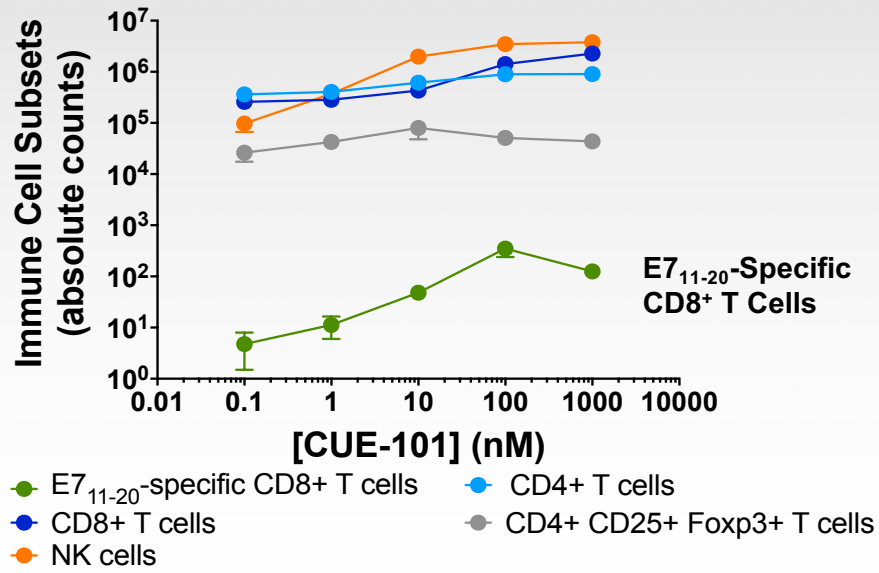
Intact & Selective Effector Function



CUE-101 specifically targets and activates HPV-E7 T cells

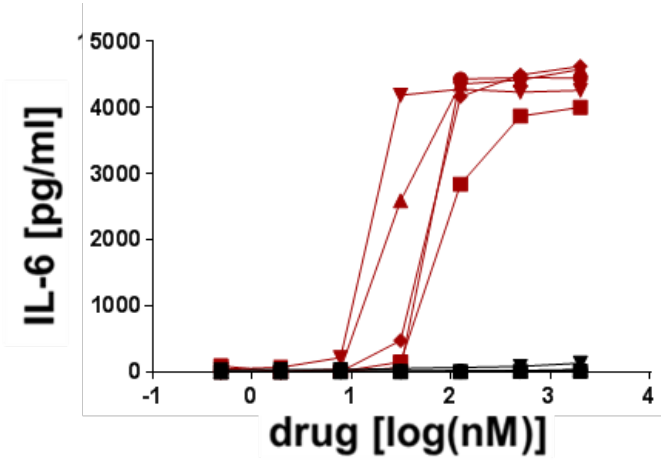
CUE-101: *In Vitro* Expansion of HPV E7-Specific T Cells

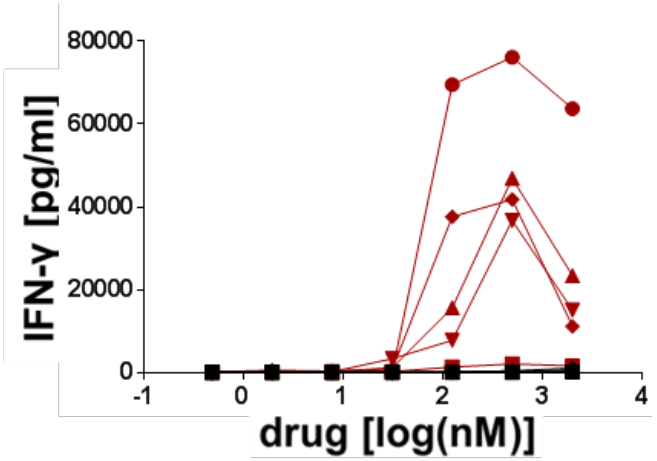


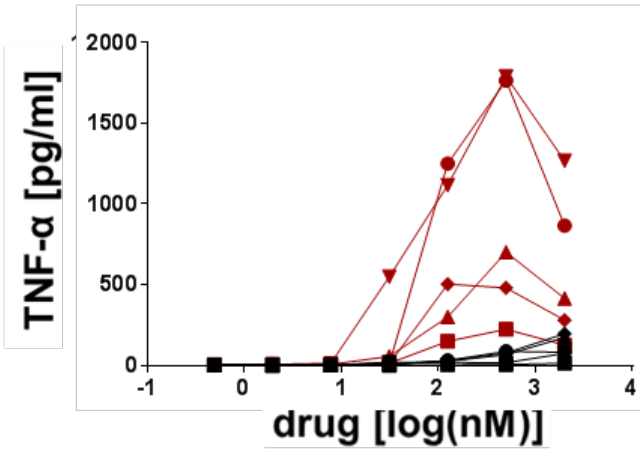


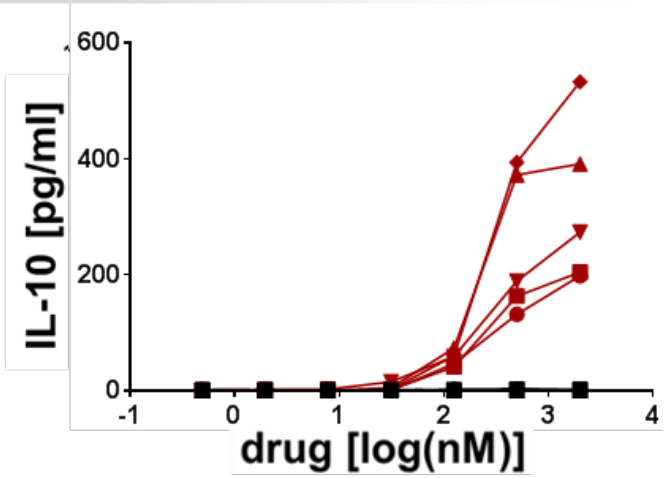
CUE-101 selectively expands HPV-E7 T cells with minimal effects on regulatory T cells

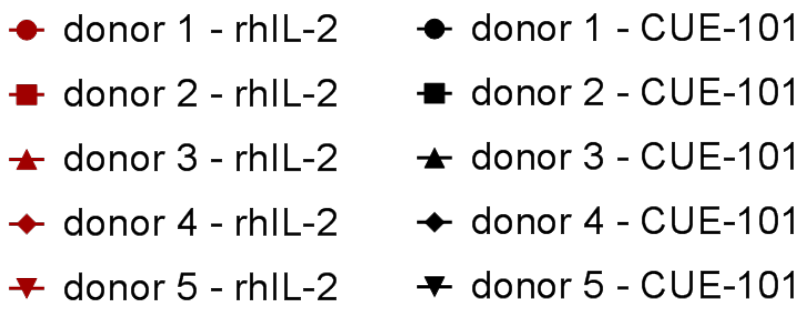
CUE-101: Mitigating the Risk Associated with Systemic WT IL-2 Activation





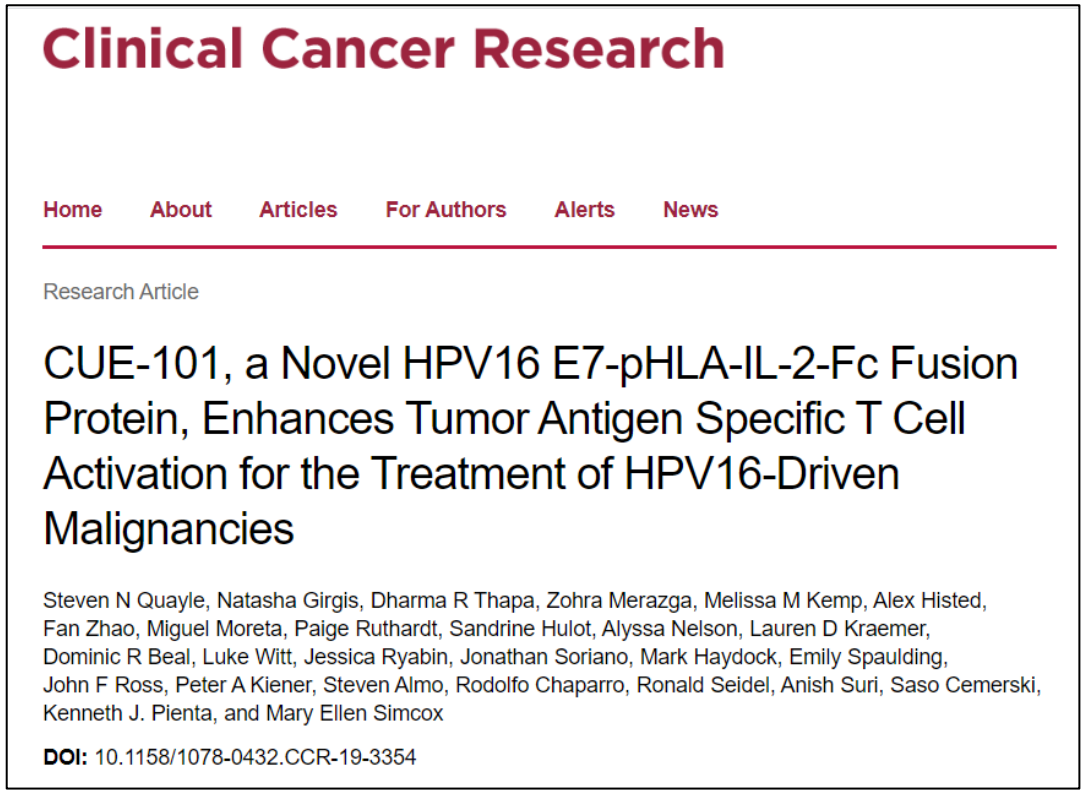






- **PBMC from healthy human donors were stimulated for 18 hours with increasing amounts of CUE-101 or recombinant human IL-2**
- **Cytokine production was assessed in culture supernatant by MSD**

CUE-101: Foundational Data Published in CCR



Clinical Cancer Research

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Research Article

CUE-101, a Novel HPV16 E7-pHLA-IL-2-Fc Fusion Protein, Enhances Tumor Antigen Specific T Cell Activation for the Treatment of HPV16-Driven Malignancies

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

DOI: 10.1158/1078-0432.CCR-19-3354

In Vitro

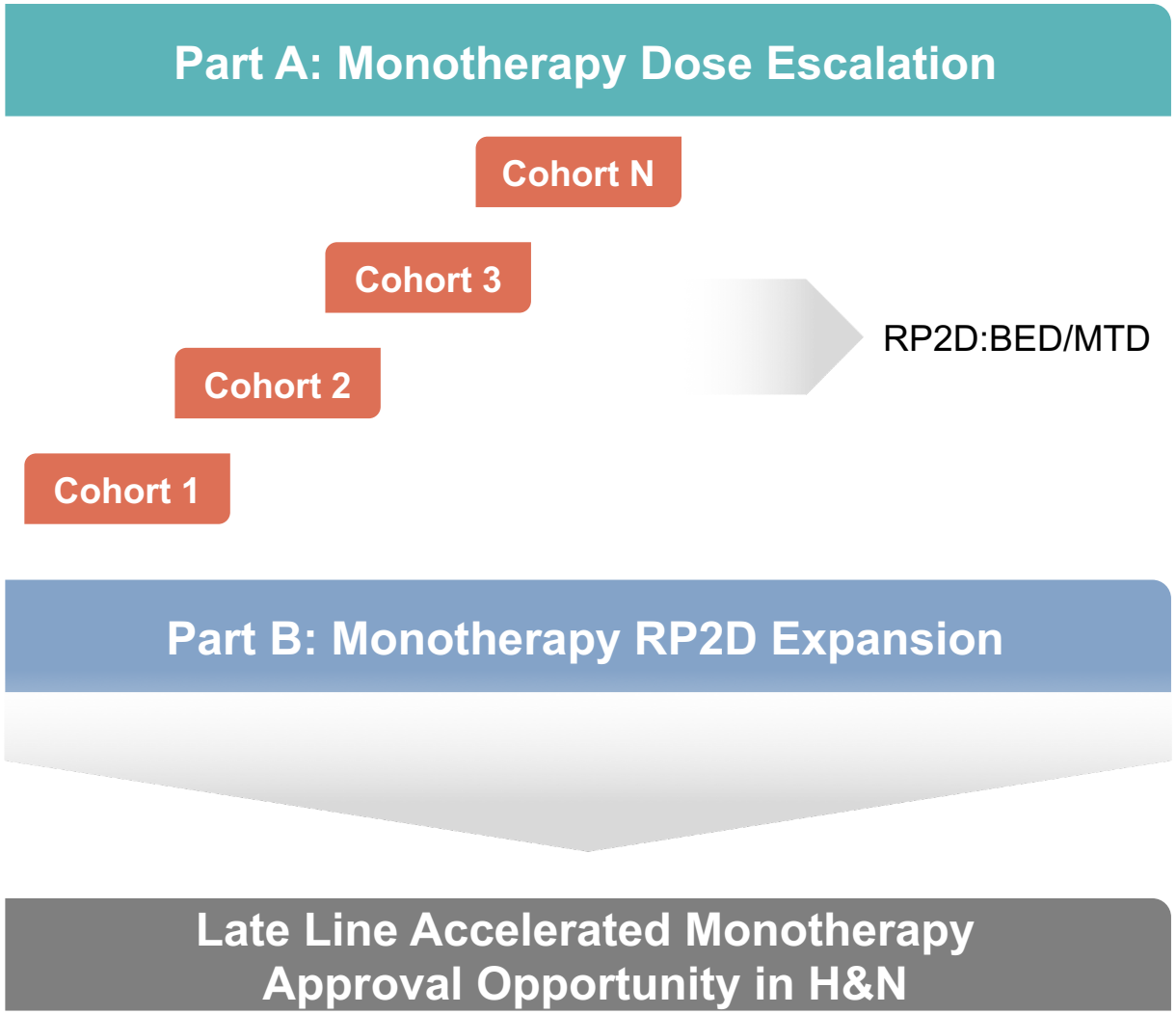
- ✓ Selective binding to HPV-specific CD8+ T cells
- ✓ Dose-dependent induction of effector function
- ✓ Expansion of HPV E7 T cells from human PBMCs
- ✓ Mitigation of risk associated with systemic IL-2 activation

Animal Model

- ✓ Selective expansion of HPV E7 CD8+ T cells in the tumor and in the periphery
- ✓ Inhibition of tumor growth and survival in TC-1 syngeneic model, both as a monotherapy and in combination with anti-PD-1
- ✓ Generation of immunologic memory against TC-1 tumor cells (i.e., re-challenge study)

Note: Publications and posters are available on the Investor Relations section of the Cue Biopharma website

CUE-101: Ongoing First-In-Human Study



- **Design** (CUE-101 Q3W)
  - Part A: Dose Escalation (3+3)
  - Part A: Safety Expansion (Up to 9 Patients)
  - Part B: Dose Expansion (10-20 Pts at RP2D)
- **Eligibility**
  - Part A & B: HPV+ H&N Cancer, R/M 2L+
- **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

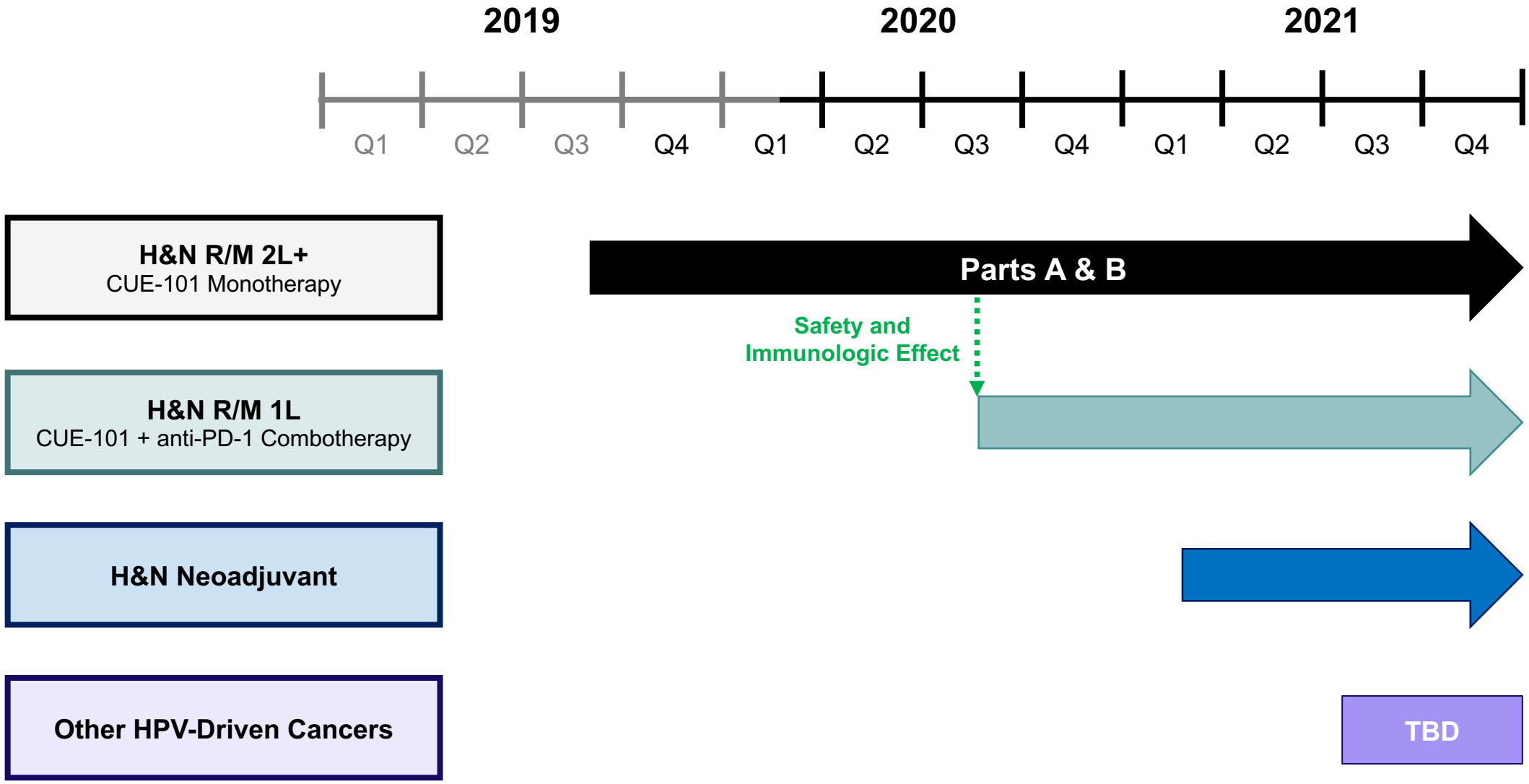
CUE-101: Phase I Clinical Development Network

- **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
- **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

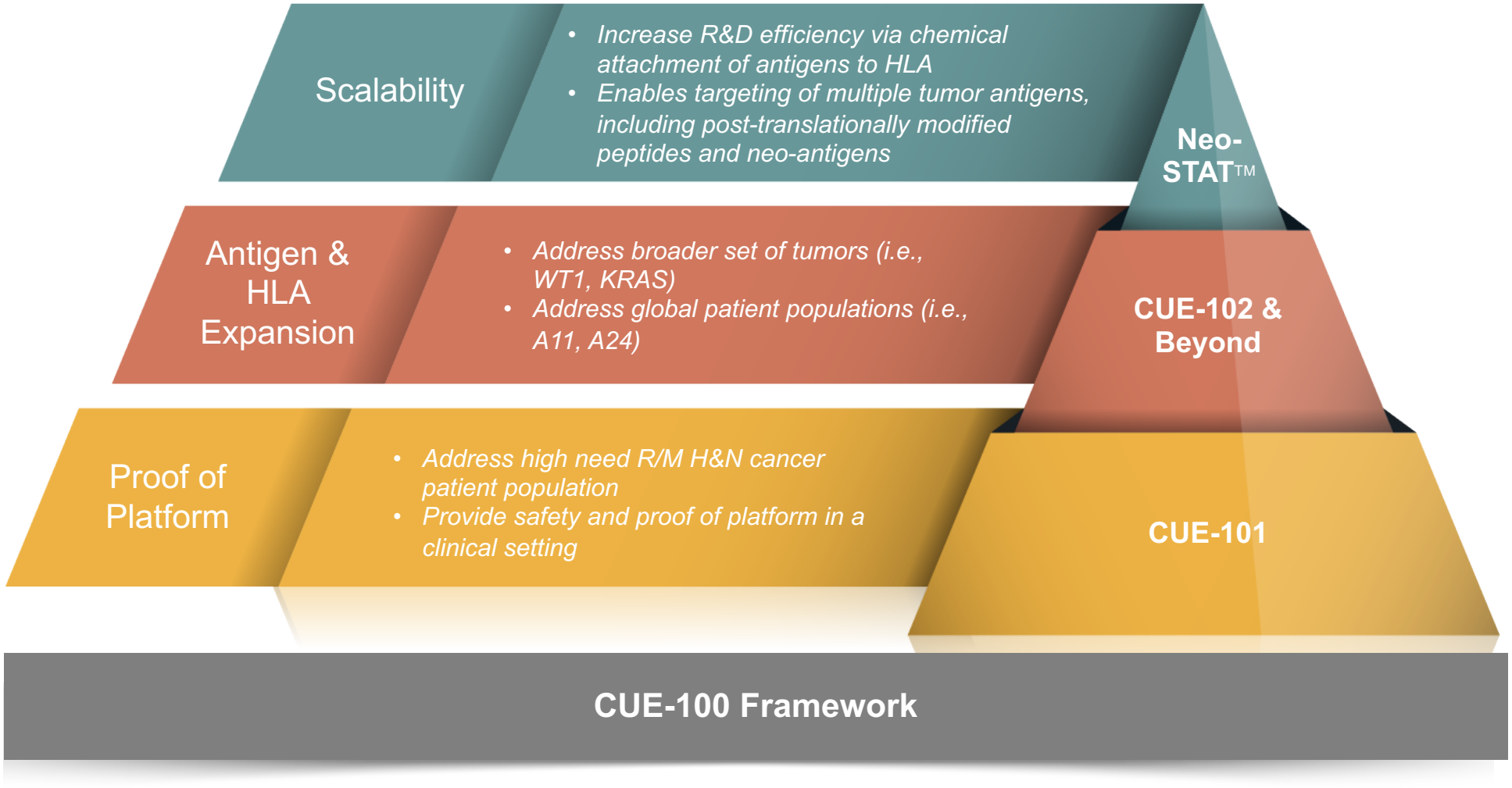
Cue has engaged a network of nationally recognized clinical investigators and 12 Phase I sites are now open

CUE BIOPHARMA

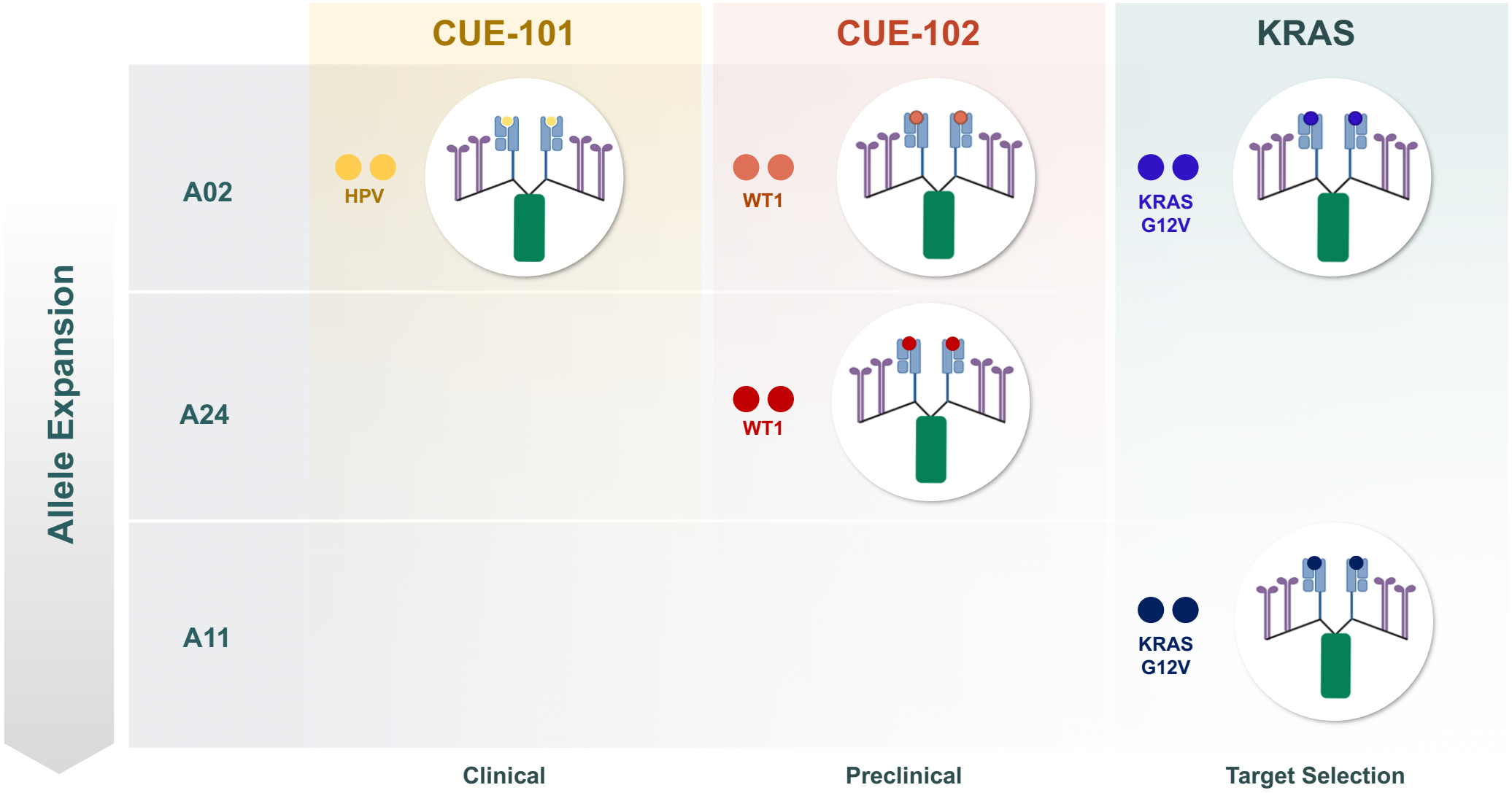
CUE-101: Clinical Development Plan



Building Blocks of IO Growth Strategy

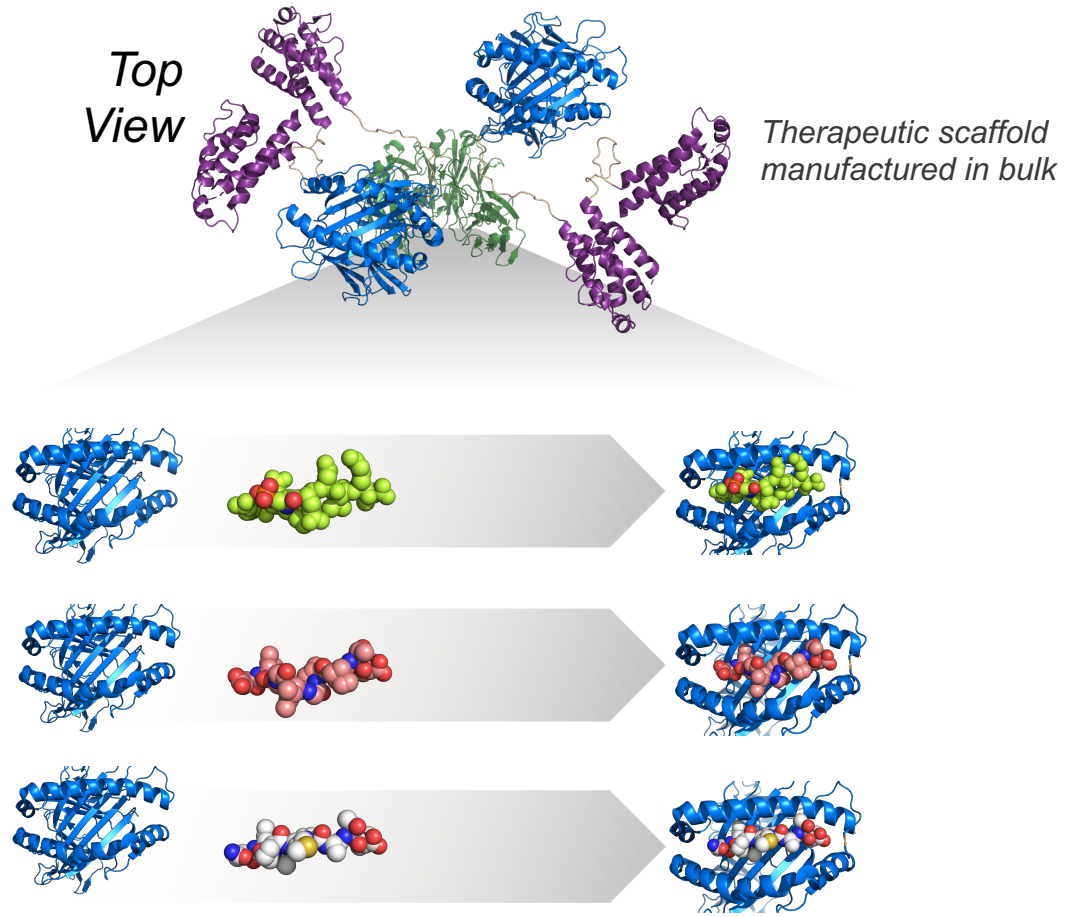


CUE-100 Series Extensibility: CUE-102 and KRAS



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

CUE-100 Neo-STAT

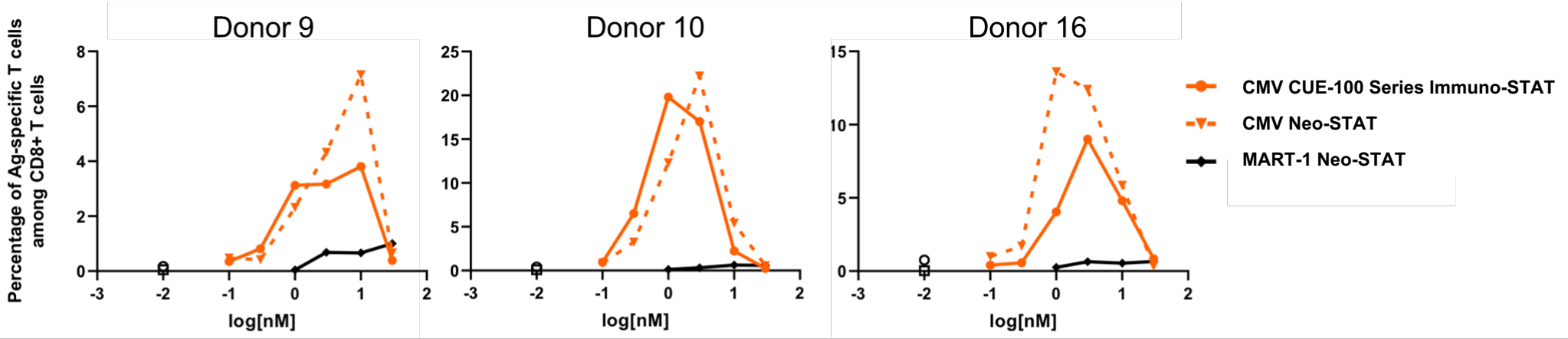


Therapeutic scaffold receptive for chemical conjugation of peptides, that potentially:

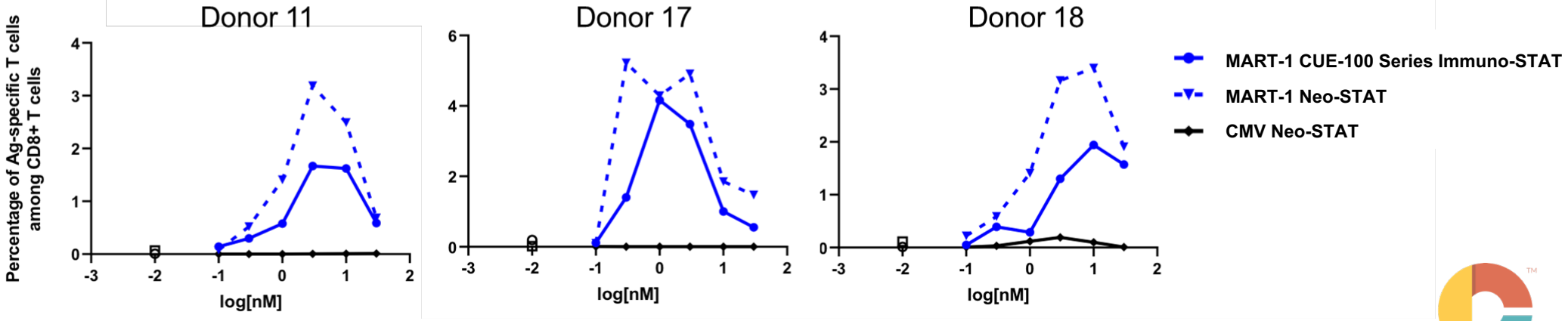
- **Increases R&D efficiency** and reduces cost of the generation of clinical grade material on the CUE-100 framework
- **Enables targeting of multiple tumor antigens** including post-translationally modified peptides and neo-antigens for personalized therapy

Neo-STAT Driven T cell Expansion is Comparable to the Immuno-STAT Format

CMV Responsive Donors



MART-1 Responsive Donors



Restoring Immune Balance

Autoimmune Disease

Over Stimulation

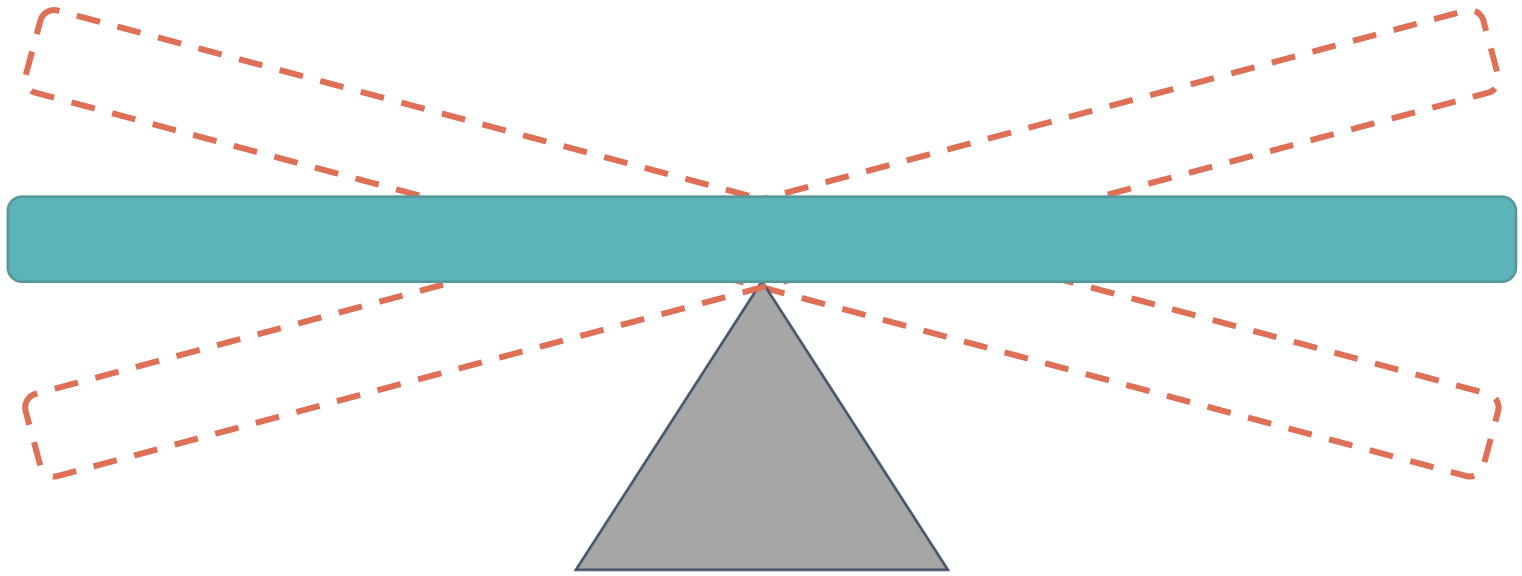
Requires inhibition of pathogenic effector T cells and/or selective activation of Tregs

Balance

Suppression

Requires expansion of tumor-specific effector T cells or reversal of exhausted T cells

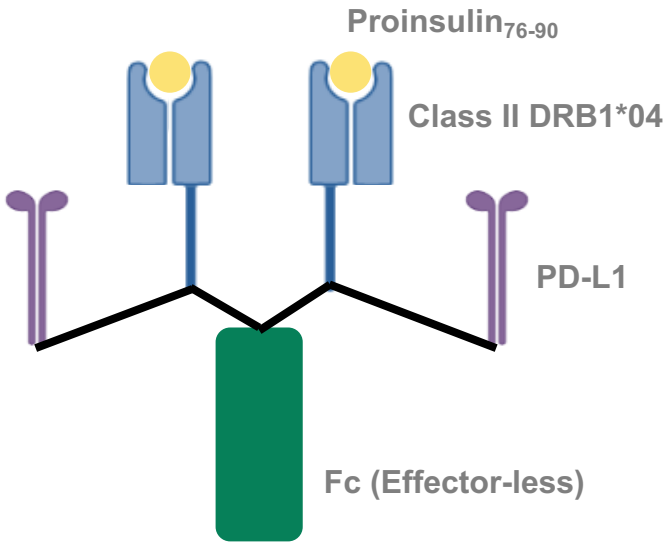
Cancer & Infection

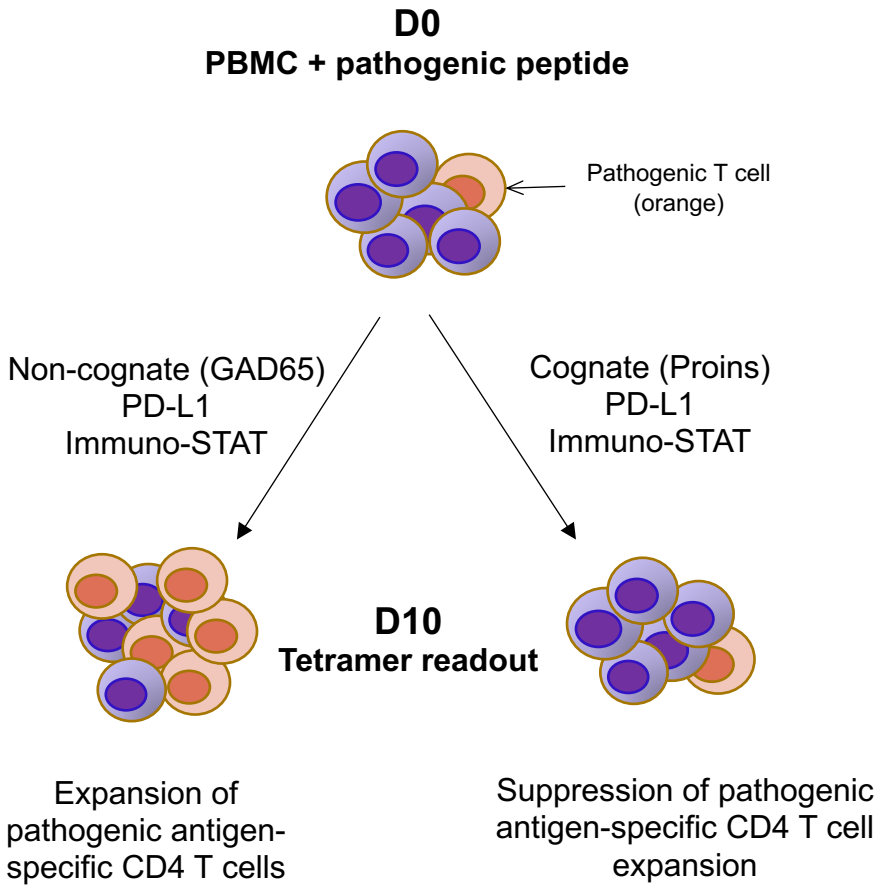


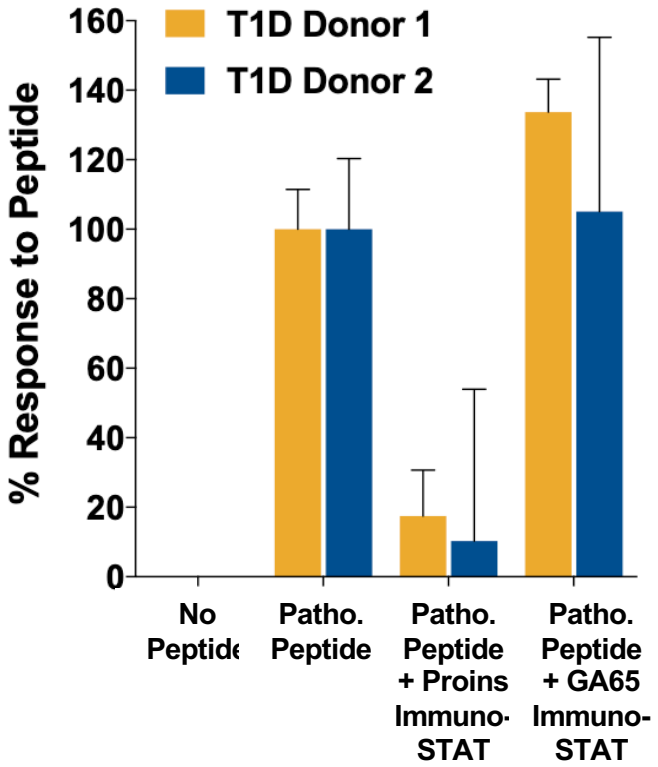
Outside of immuno-oncology, Cue has partnered with Merck to establish Immuno-STAT applications in autoimmune diseases

CUE BIOPHARMA

Immuno-STAT Dampens Autoreactive CD4+ T cells

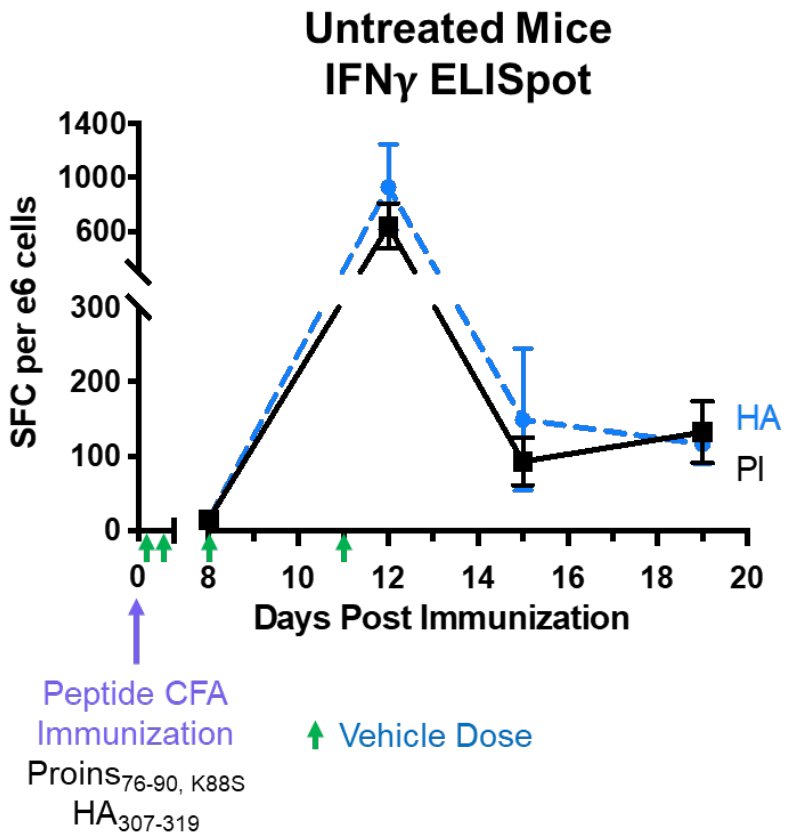


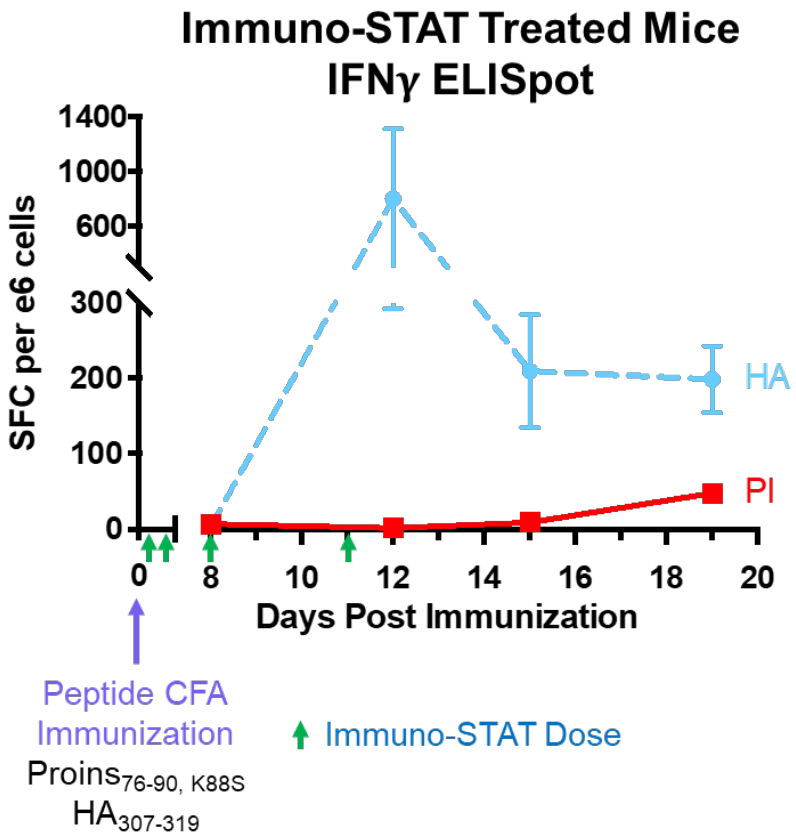




Proins$_{76\text{-}90,\ K88S}$/DR4-PDL1 Immuno-STAT selectively inhibits antigen-specific CD4^{+} T Cell expansion from PBMCs of T1D donors

Early Intervention with Immuno-STAT Selectively Reduces Proinsulin Responsive CD4+ T Cells in Transgenic Mice





Treatment with Immuno-STAT starting on Day 1 post immunization selectively suppresses expansion of PI-reactive cells without inhibiting expansion of HA-reactive cells

Note: $HA_{307-319}$ is a well-characterized viral antigen used as an experimental control

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Focused Execution Against Platform Validation

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