UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): March 18, 2021

Cue Biopharma, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-38327**	**47-3324577**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

21 Erie St., Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

(Registrant's telephone number, including area code): (617) 949-2680

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	**CUE**	**The Nasdaq Stock Market LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 7.01 Regulation FD Disclosure.

On March 18, 2021, Cue Biopharma, Inc. (the "Company") will be presenting at the Oppenheimer 31st Annual Healthcare Conference. A copy of the Company's corporate presentation made at the conference is attached to this Current Report on Form 8-K as Exhibit 99.1 and is incorporated by reference into this Item 7.01.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

d) Exhibits

Exhibit No.	Description
99.1	Cue Biopharma, Inc. Corporate Presentation, dated March 18, 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Cue Biopharma, Inc.

Date: March 18, 2021

By: /s/ Daniel R. Passeri
Name: Daniel R. Passeri
Title: Chief Executive Officer

Exhibit 99

Corporate Presentation

Immune Responses, On Cue™

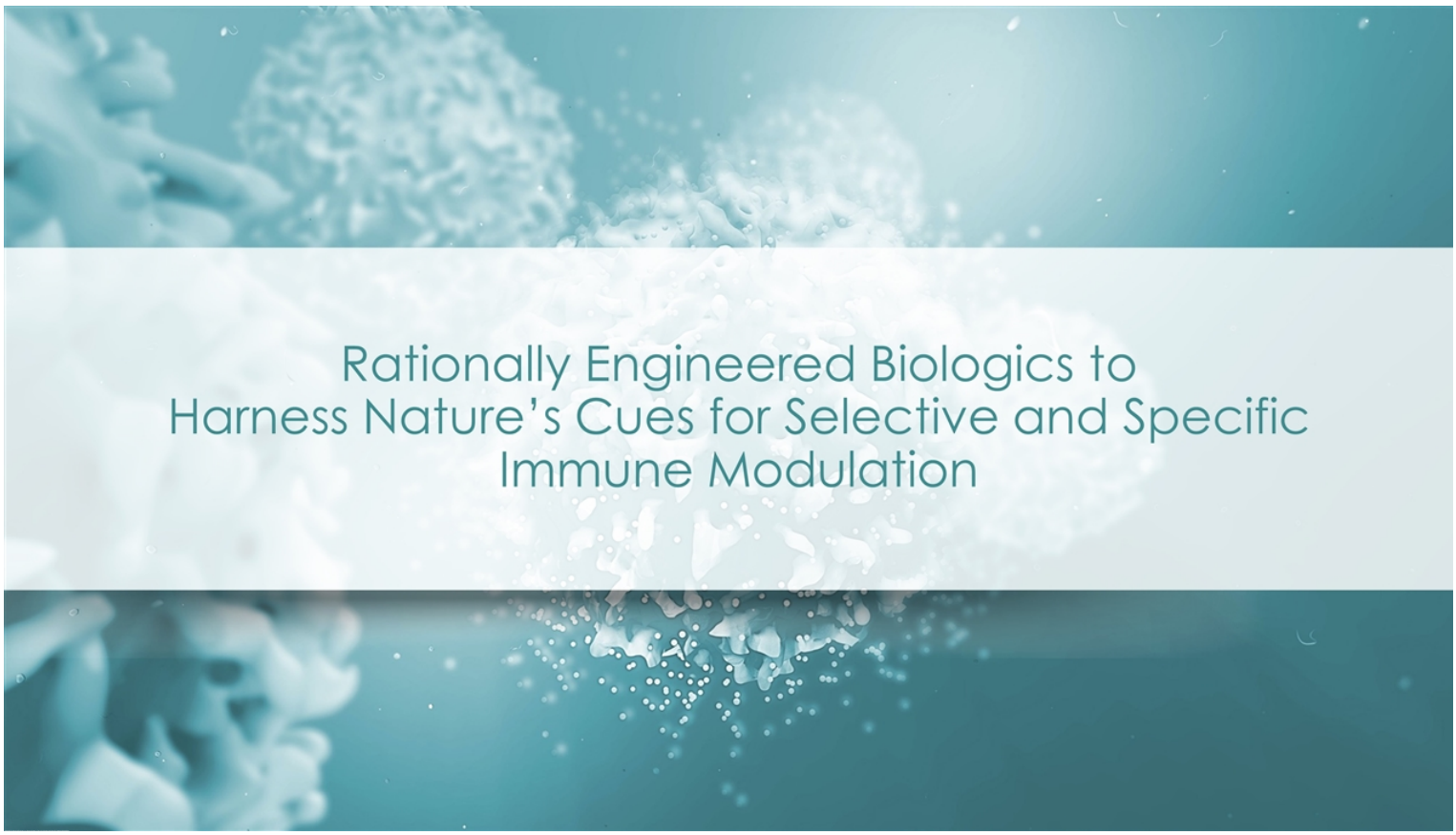
Nasdaq: CUE

Oppenheimer 31st Annual Healthcare Conference, March 18, 2021

Forward-Looking Statements Disclaimer

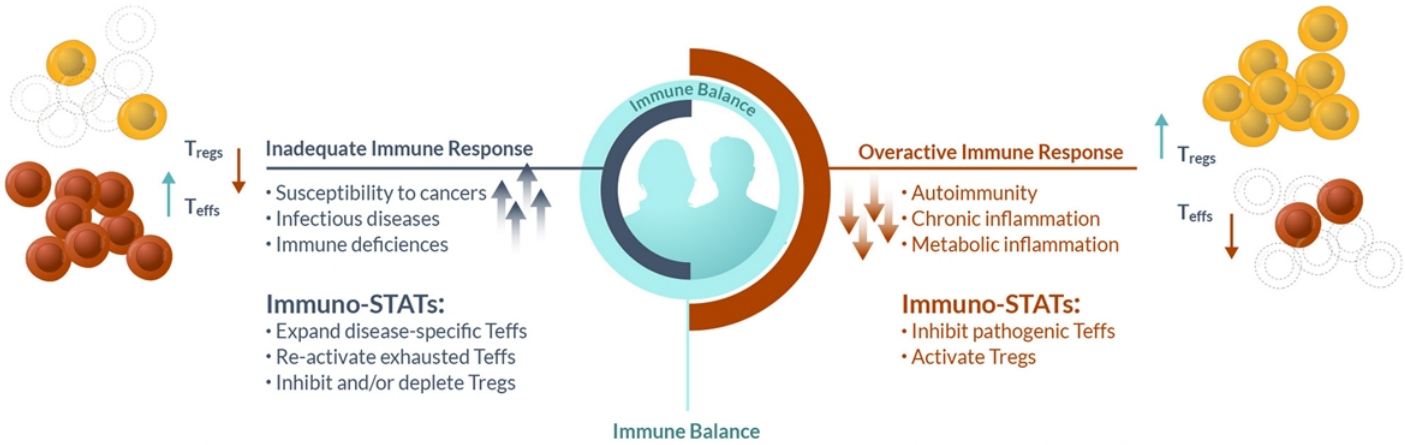
This presentation has been prepared by Cue Biopharma, Inc. ("we," "us," "our," "Cue" or the "Company") and is made for informational purposes only and does not constitute an offer to sell or a solicitation of an offer to buy securities, nor shall there be any sale of any securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. The information set forth herein does not purport to be complete or to contain all of the information you may desire. Statements contained herein are made as of the date of this presentation unless stated otherwise, and neither this presentation, nor any sale of securities, shall under any circumstances create an implication that the information contained herein is correct as of any time after such date or that information will be updated or revised to reflect information that subsequently becomes available or changes occurring after the date hereof.

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, "vision", "likely" or other comparable terms. All statements other than statements of historical facts included in this presentation 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 our development plans for CUE-101 and the continued buildout of our pipeline, the sufficiency of our cash, cash equivalents and marketable securities to support the clinical development of CUE-101, 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; potential setbacks in our research and development efforts including negative or inconclusive results from our preclinical studies, 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; adverse effects caused by public health pandemics, including COVID-19, including possible effects on our operations and clinical trials; 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, collaborators, contract research organizations, suppliers and other business partners; our ability to obtain adequate financing to fund our business operations in the future; our ability to maintain and enforce necessary patent and other intellectual property protection, competitive factors, general economic and market conditions; 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.



Rationally Engineered Biologics to Harness Nature's Cues for Selective and Specific Immune Modulation

Restoring Immune Balance

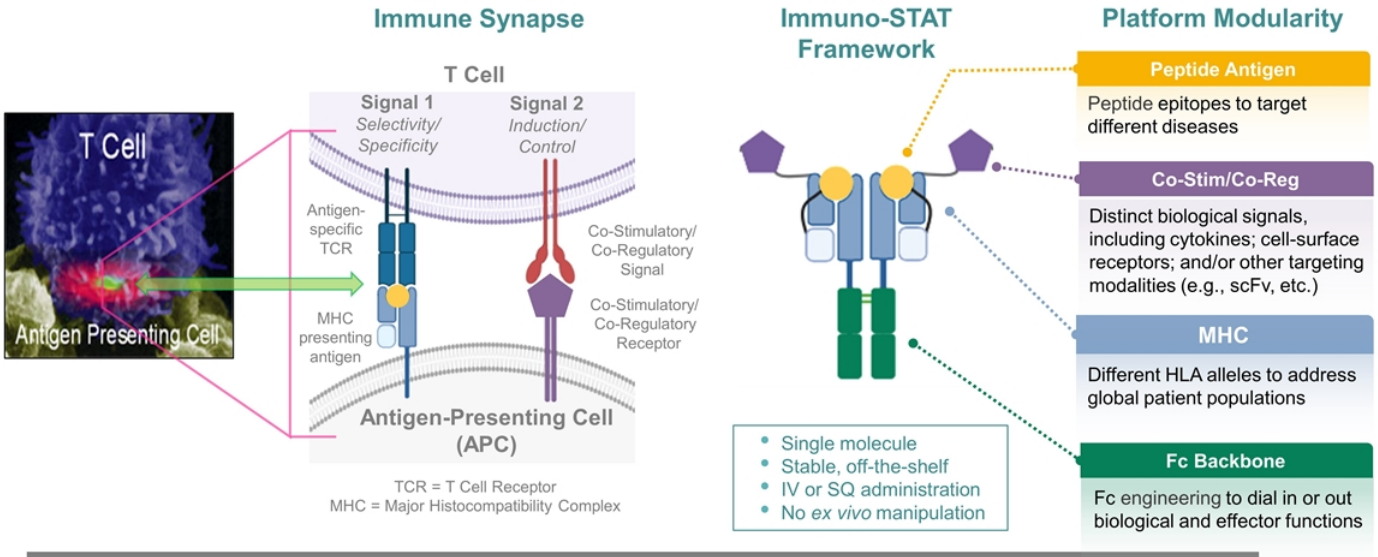


Immune Balance

Restoration of immune balance is a key pillar of human health

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

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

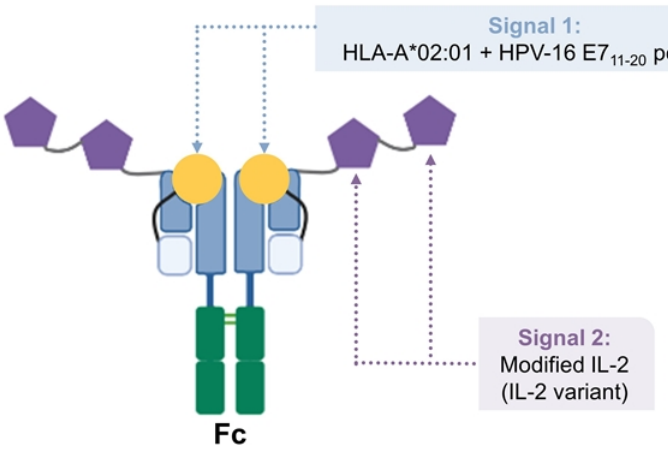


The Immuno-STAT platform has the potential to generate a diversity of therapeutic molecules to selectively target and modulate the activity of a broad range of disease-relevant T cells

Source: Dustin, Cancer Immunol Res 2014

CUE-101: Designed to Selectively Prime and Expand HPV-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 HPV-16 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+

CUE-101: Phase 1 Clinical Development Network

Cue Biopharma has engaged a network of nationally recognized clinical investigators and 14 Phase 1 sites are now open

- **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

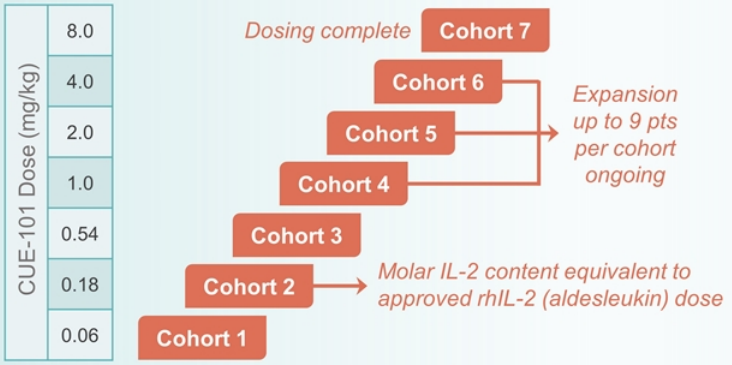
CUE-101: Ongoing Monotherapy First-In-Human Phase 1 Trial

Indication: HPV+ Recurrent or metastatic head and neck cancer with confirmed progressive disease

Heavily pretreated: Refractory or resistant to 1st line platinum-based chemotherapy and/or CPIs

Part A: Monotherapy Dose Escalation
(Q3W, 3 + 3 design, with expansion up to 9 patients per cohort)

Part B: Monotherapy Expansion
(up to 20 total patients)



Parts A & B:
Primary endpoints:
- Safety and tolerability

Secondary endpoints:
- PK/PD
- Anti-tumor activity per RECIST 1.1

ClinicalTrials.gov: NCT03978689

CUE-101 has been well tolerated through 7 cohorts with evidence of clinical activity
Currently expanding Cohort 4, 5, and 6

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: Cohort 4 Case Study – 3rd line Systemic Treatment

	Treatment	Timeline	Outcome
1	Robotic transoral resection tongue base	First intervention	Curative intent
2	Adjuvant RT	1 mo	Curative intent
3	Carboplatin + fluorouracil + cetuximab for advanced, metastatic disease	1 yr, 1 mo	Duration: 6.0 weeks **Best Response = SD**
4	RT to metastatic mass	1 yr, 4 mos	Palliation
5	Pembrolizumab for advanced, metastatic disease	2 yrs	Duration: 9.4 weeks **Best Response = PD**
6	**CUE-101 (1 mg/kg, Q3W)**	2 yrs, 5 mos	Duration: 18.1 weeks

Tolerability

ECOG Status: 0 at screening; Unchanged while on CUE-101 therapy

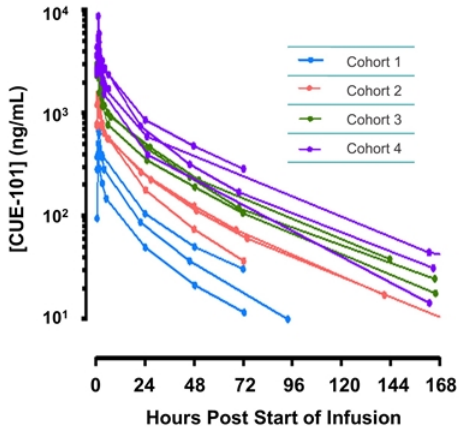
All TRAEs Grade ≤2

CUE-101 Best Response: Confirmed SD by RECIST 1.1 for 18 weeks

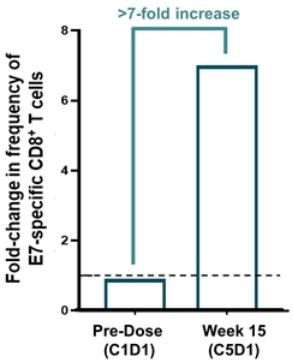
CUE BIOPHARMA

CUE-101: Cohort 4 Case Study – PK, PD, Response

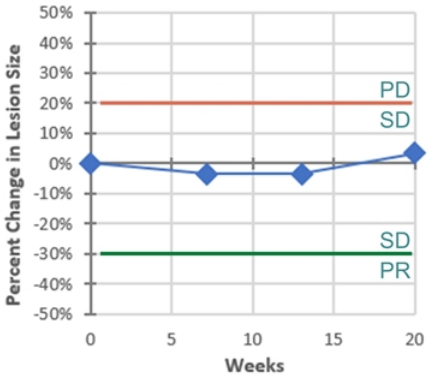
Pharmacokinetics:
Dose proportional



Pharmacodynamics:
Increase in peripheral blood E7-specific T cells



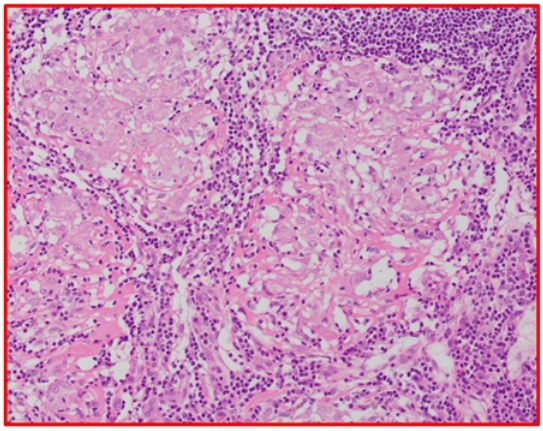
One target lesion at baseline:
Diameter: 58 mm
No change for 20 wks



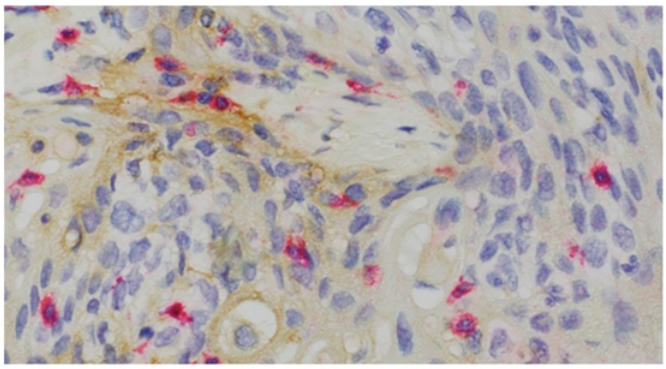
CUE-101 Best Response: Confirmed SD by RECIST 1.1 for 18 weeks

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



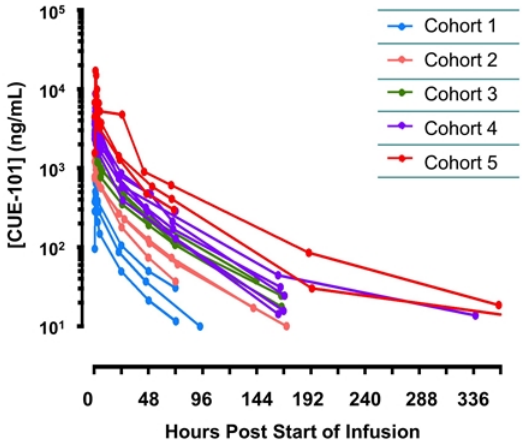
Hematoxylin and eosin stain
(cell nuclei = blue; extracellular matrix and cytoplasm = pink)



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

CUE-101: Cohort 5 Case Study – PK, Response

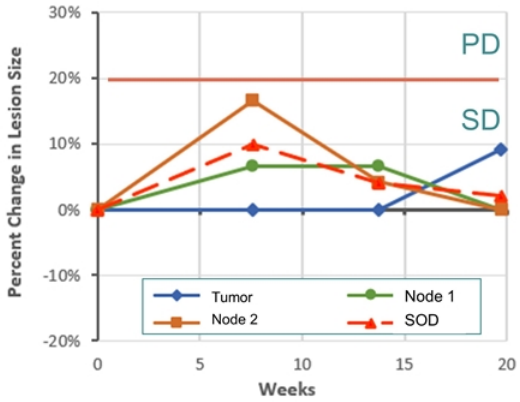
Pharmacokinetics:
Dose proportional



Three target lesions at baseline:

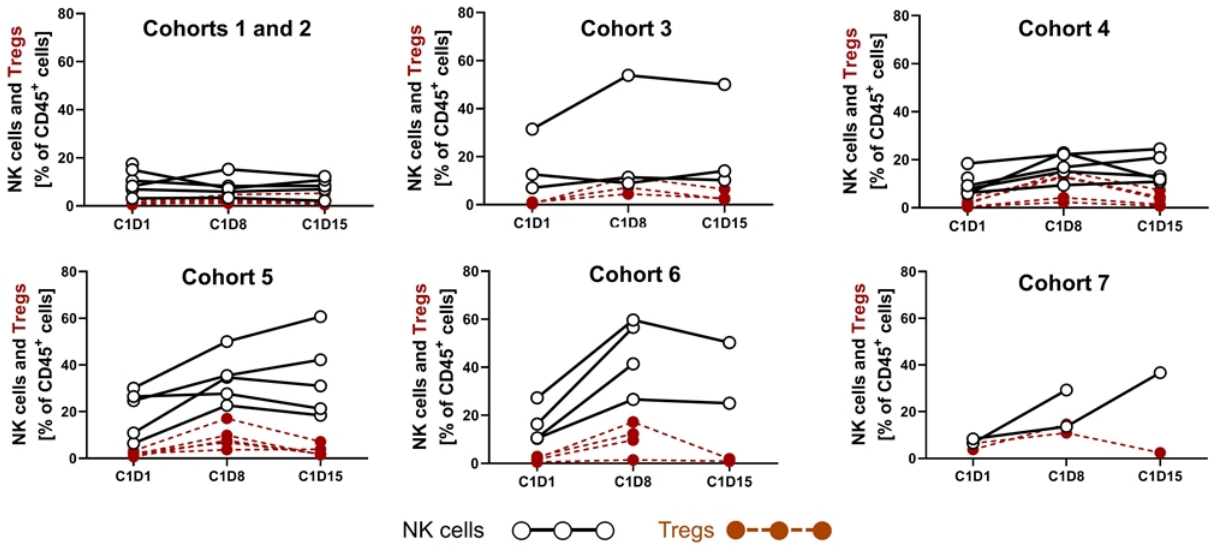
1) Tumor mass: 11 mm
2) Lymph node No.1: 15 mm
3) Lymph node No. 2: 24 mm

Sum of Diameters (SOD) = 50 mm



CUE-101 Best Response: Confirmed SD by RECIST 1.1 for 28 weeks; acquired COVID-19 and came off study

CUE-101: Induced Changes in NK Cells and Tregs in Cohorts 1 - 7



Dose-dependent, sustained increase in NKs with transient increase in Tregs, consistent with IL-2 pharmacology observed in the clinic

CUE-101: Ongoing Pembrolizumab Combination Study

ClinicalTrials.gov:
NCT03978689

Eligibility:
- HPV+ Head and neck cancer
- Recurrent or metastatic (R/M)
- 1st Line
- HLA-A*0201 genotype
- Life expectancy ≥ 12 weeks
- Eligible for pembrolizumab in the first-line setting

Part C: Pembrolizumab Combination Dose Escalation

Initiated February 2021

Pembrolizumab 200 mg, Q3W	CUE-101 Dose (mg/kg)
	4.0
	2.0
	1.0

Cohort 3

Cohort 2

Cohort 1 → *Same dose of CUE-101 as in Cohort 4 in the monotherapy trial*

Part D: Combination Expansion at RP2D Dose

Design:
- Dosing Q3W
- Part C: 3 + 3 Dose escalation with 1-week safety follow up of 1st patient required at each dose prior to dosing patients 2 and 3
- Part C: PD and activity expansion up to 9 patients
- Part D: Expansion to total of 10-20 patients at RP2D

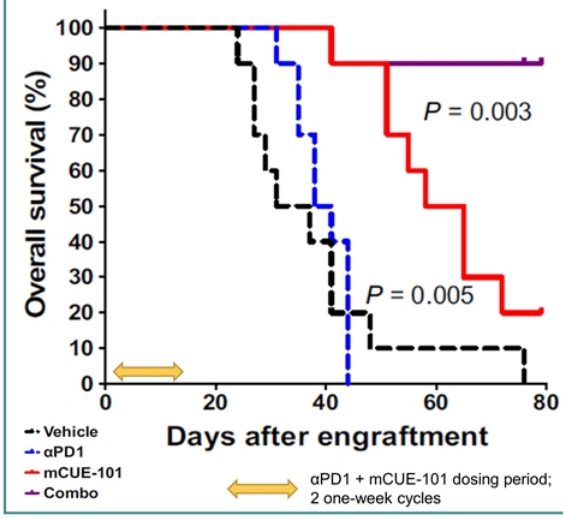
Objectives:
- *Primary:* Safety and tolerability
- *Secondary:* PK/PD, Anti-tumor activity

Biomarkers: (Pre/Post CUE-101 dose)
- HPV E7-specific CD8+ T cell counts and functionality
- Immunophenotyping, cytokine release, and TCR sequencing

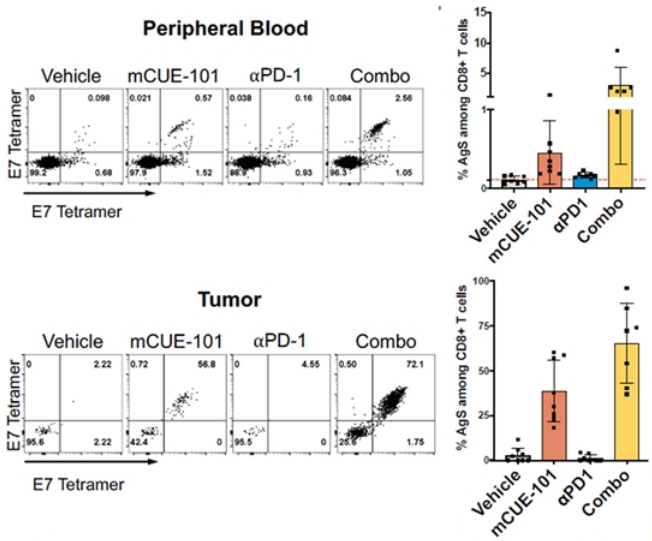
Abbreviations: PD, pharmacodynamics; PK, pharmacokinetics; RP2D, Recommended Phase 2 Dose

CUE-101: Preclinical Studies Support Pembrolizumab Combination

Tumor growth inhibition by mCUE-101 is greatly enhanced in combination with αPD1 blockade



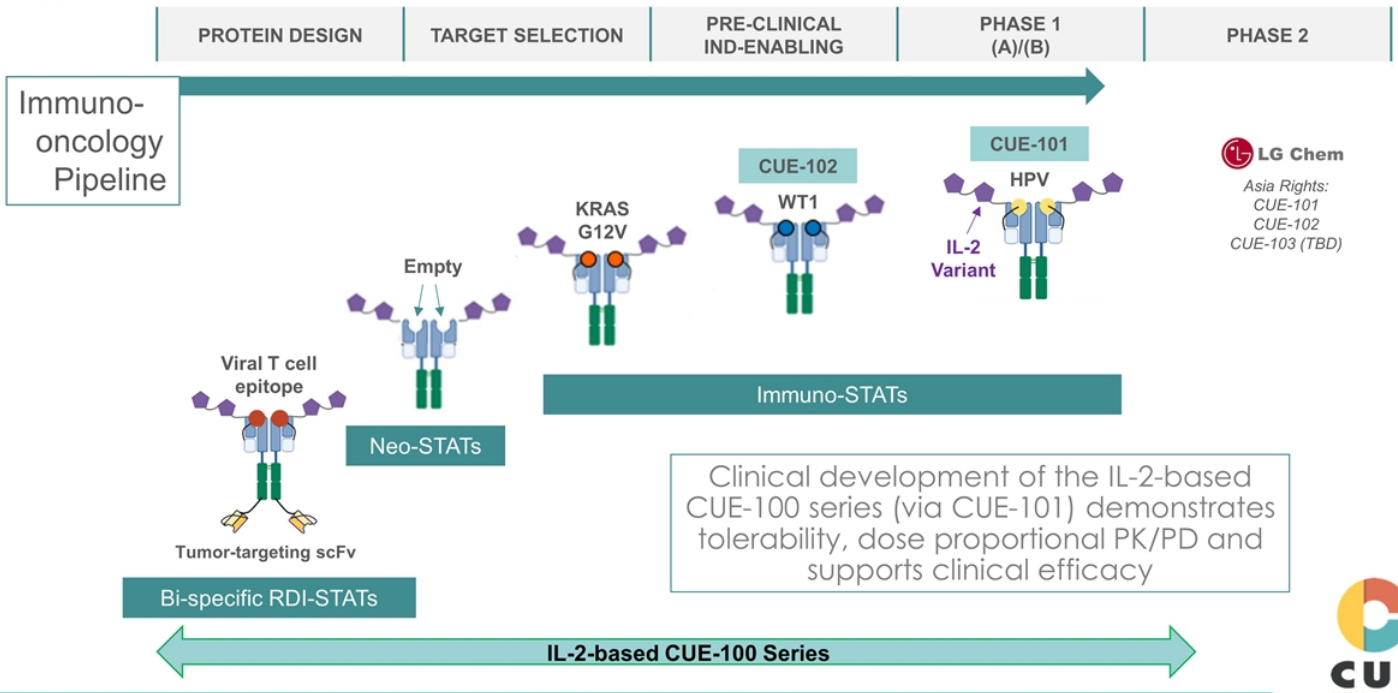
Expansion of functional HPV E7 antigen-specific CD8+ T cells in the tumor and periphery by mCUE-101 is greatly enhanced in combination with αPD1 blockade



Source: *Quayle SN, Girgis N, et al. Clin Canc Res 26:1953-64, 2020.*

Abbreviations: AgS, antigen-specific; mCUE-101, mouse surrogate of human CUE-101; αPD1, anti-PD1 surrogate

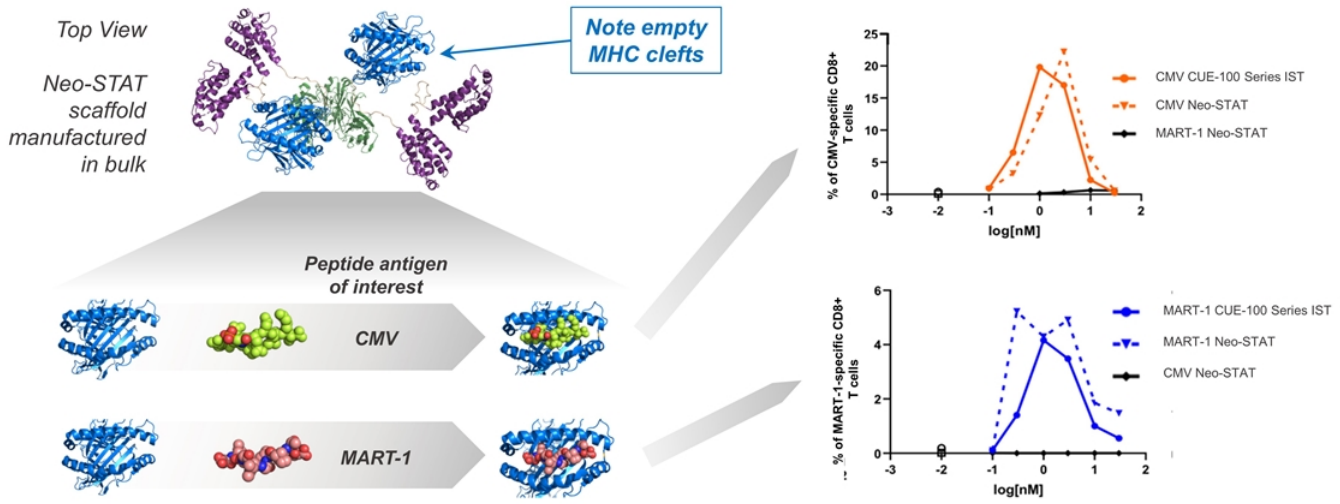
CUE-101, CUE-100 Series and Derivatives



Clinical development of the IL-2-based CUE-100 series (via CUE-101) demonstrates tolerability, dose proportional PK/PD and supports clinical efficacy

IL-2-based CUE-100 Series

CUE-100 Neo-STAT: Addresses Tumor Heterogeneity



Potential Therapeutic Applications to include:

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

RDI-STATs: Novel Bi-specifics Re-directing Viral-Specific T Cells to Tumor Cells

ARTICLE

https://doi.org/10.1038/s41467-019-08534-1 OPEN

Virus-specific memory T cells populate tumors and can be repurposed for tumor immunotherapy

Pamela C. Rosato[1], Sathi Wijeyesinghe[1], J. Michael Stolley[1], Christine E. Nelson[1], Rachel L. Davis[1], Luke S. Manlove[1], Christopher A. Pennell[2], Bruce R. Blazar[3], Clark C. Chen[4], Melissa A. Geller[5], Vaiva Vezys[1] & David Masopust[1]

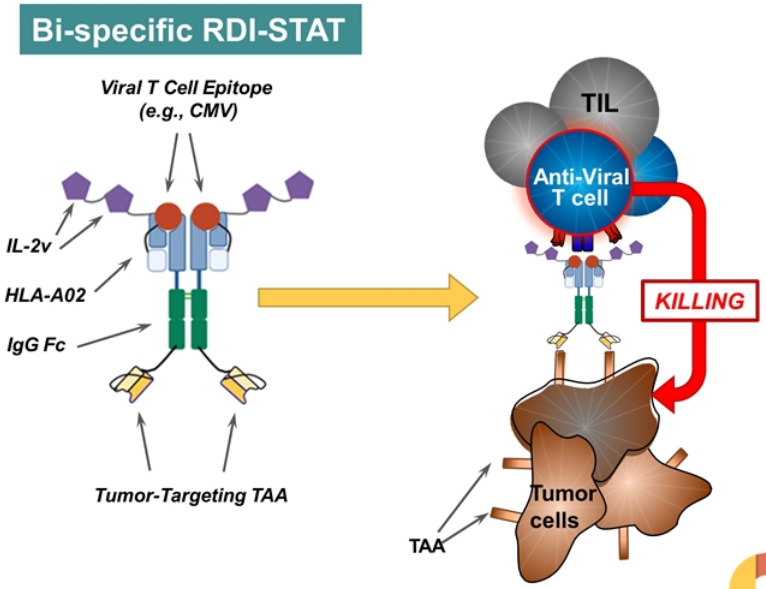
LETTER

https://doi.org/10.1038/s41586-018-0130-2

Bystander CD8$^+$ T cells are abundant and phenotypically distinct in human tumour infiltrates

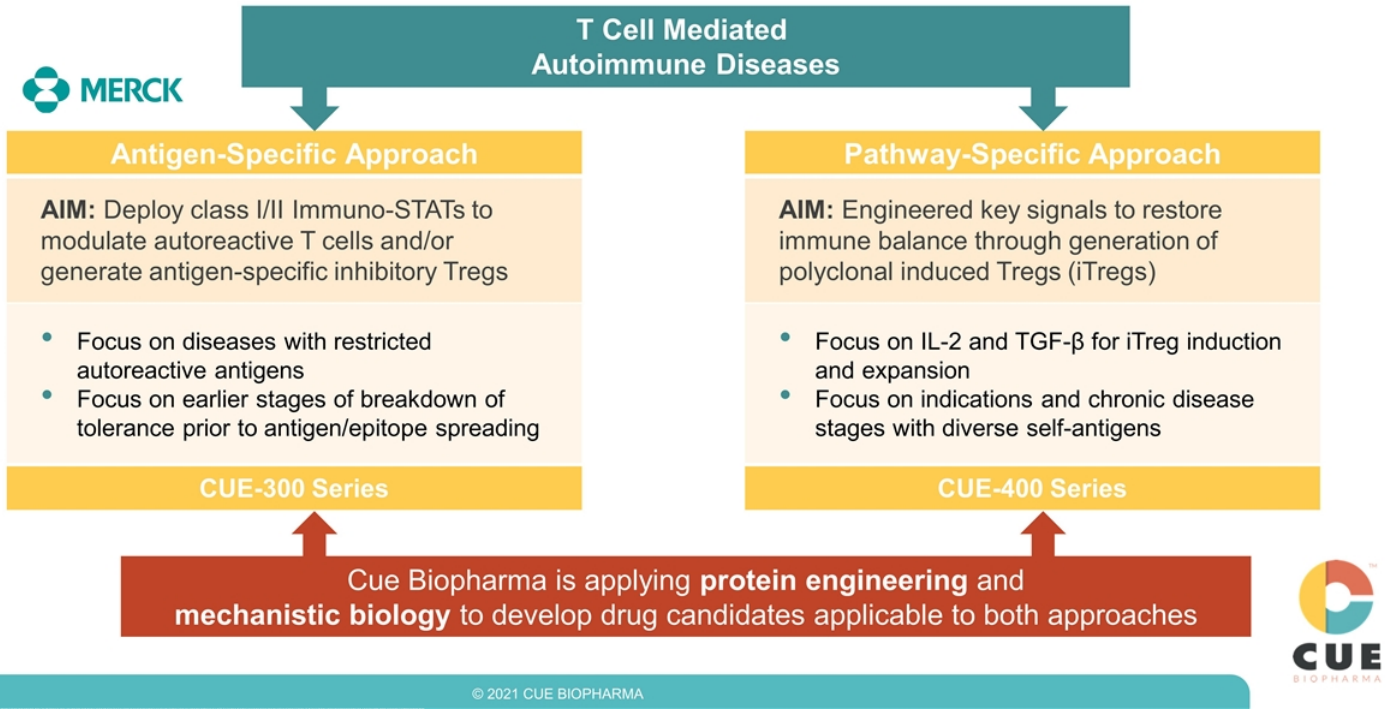
Yannick Simoni[1*], Etienne Becht[2], Michael Fehlings[1,3], Chiew Yee Loh[1], Si-Lin Koo[2], Karen Wei Weng Teng[4], Ivo Poh Sheng Yeong[4,5], Rahul Nahar[6], Tong Zhang[4], Hussein Kared[7], Kaibo Duan[7], Nicholas Ang[8], Michael Poidinger[1], Yin Yeng Lee[1], Anis Larbi[1], Alexis J. Khng[9], Emile Tan[9], Cherylin Fu[9], Ronnie Mathew[9], Melissa Teo[9], Wan Teck Lim[9], Choe Kerong Toh[9], Boon-Hean Ong[9], Tina Kuh[7], Axel M. Hillmer[2], Angela Takano[9], Tony Kiat Hon Lim[4,5,9], Eng Huat Tan[9], Weiwei Zhai[2], Daniel S. W. Tan[3,5], Iain Beehuat Tan[3,5,9] & Evan W. Newell[1*]

- **Harnesses** a pre-existing and robust viral T cell repertoire present in high frequency
- **Superior specificity:** avoids systemic activation of ALL T cells
- **Superior safety:** minimizes cytokine release
- **De-risked** by CUE-101 clinical experience



CMV, cytomegalovirus; TAA, tumor-associated antigen; TIL, tumor-infiltrating lymphocyte

Approaches to Modulate Autoreactive T Cell Responses

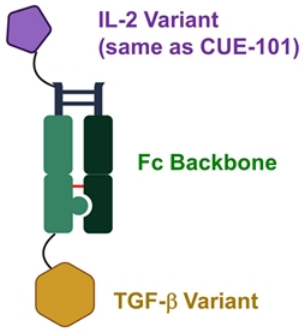


CUE-401: Immune Balance Restoration via Induced Tregs (iTregs)

Advantages for iTregs vs. nTregs

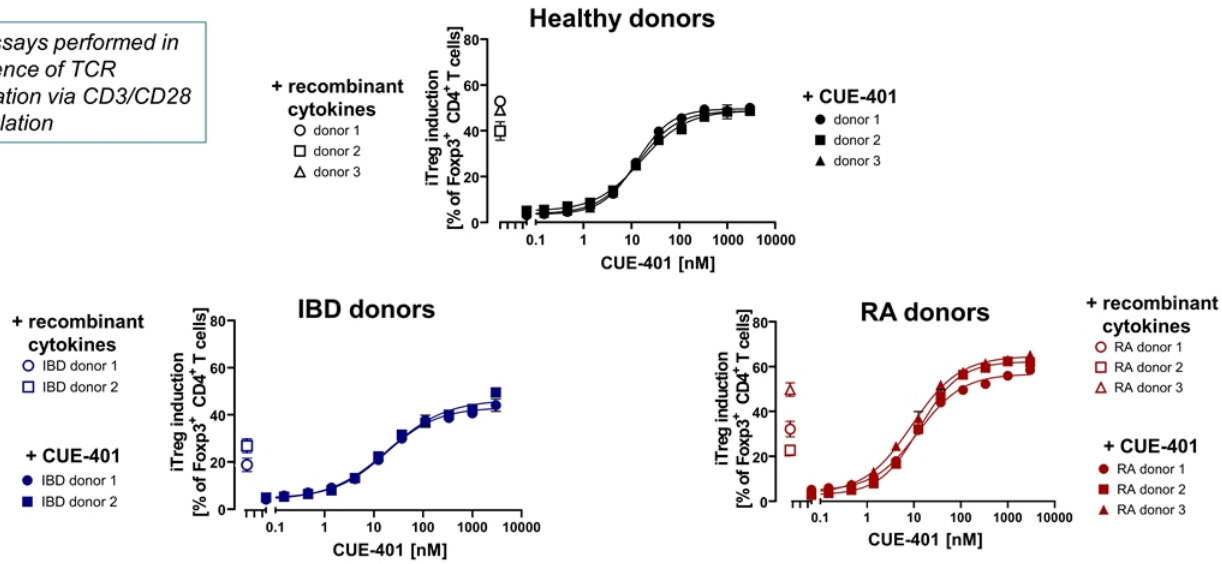
- **Numbers**: nTregs are limited in numbers vs iTregs, which can be generated from the broader CD4+ T cell repertoire
- **Diversity**: TCR specificity of nTregs is pre-determined and fixed, while iTregs can be generated from vastly diverse polyclonal CD4+ T cells
- **Phenotype**: regulatory phenotype of iTregs can be achieved and sustained via IL-2 and TGF-beta signals
- **Disease impact**: Conversion of pathogenic T cells into regulatory phenotype is an attractive therapeutic strategy for immune re-set
- **Application**: Broad applications for iTregs in numerous autoimmune diseases, GVHD and transplantation

CUE-401



CUE-401: Induction of FoxP3+ iTregs

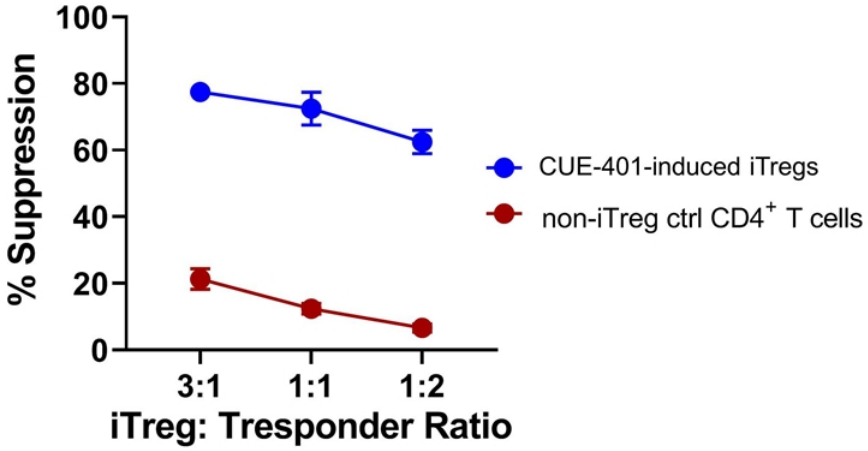
All assays performed in presence of TCR activation via CD3/CD28 stimulation



CUE-401 enhances iTregs as measured by induction of expression of the master Treg transcription factor FoxP3

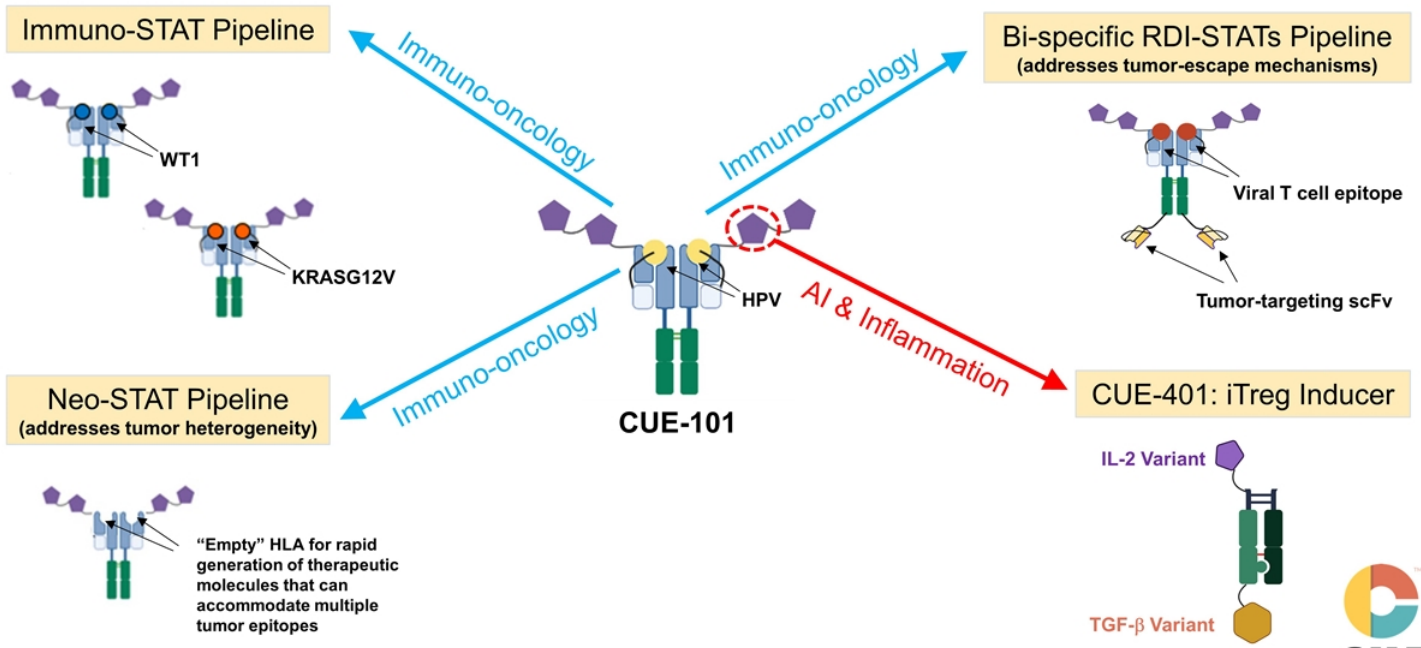
CUE-401: Suppression of T Cell Responses by iTregs Induced by CUE-401

iTreg suppression of polyclonal T cell proliferation

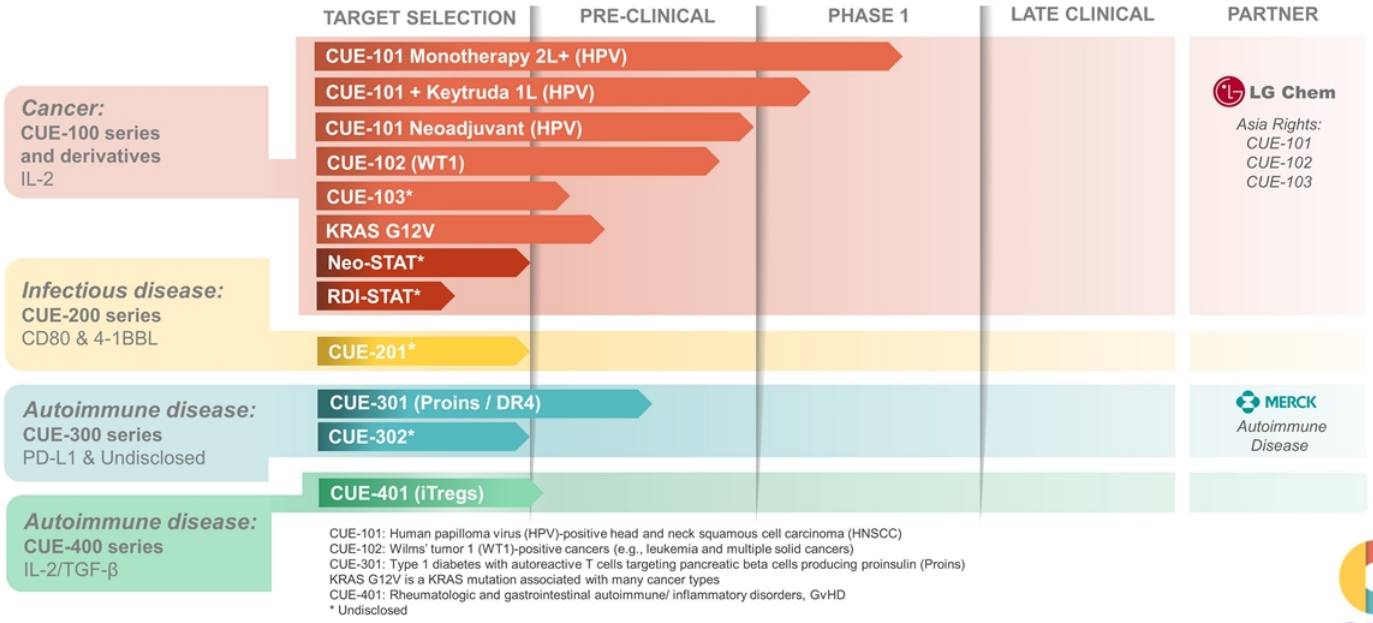


Average of 3 donors
% suppression compared to T responder alone

CUE-101 Experience: Potential for Broad Opportunities in IO and AI



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

Key 2021 Anticipated Milestones: Risk Reduction and Value Creation

1. Select CUE-101 monotherapy recommended Phase 2 dose in **mid-2021**
2. Report initial results of CUE-101 + pembrolizumab Phase 1 combination trial in **2H21**
3. Initiate CUE-101 neoadjuvant study to enable intratumor PD **in 2H21**
4. Continue CUE-102 IND-enabling studies with IND filing in **1H22**
5. Initiate & expand KRAS G12V, & Neo-STAT CMC activities in **2H21**
6. Achieve optimization of lead candidate for CUE-301 in **2H21**
7. CUE-401 Preclinical validation of iTreg function in **2H21**

We believe our cash, cash equivalents and marketable securities at December 31, 2020 are sufficient to support CUE-101 clinical proof of concept and pipeline advancement into the third quarter of 2022


CUE
BIOPHARMA
Thank you
Immune Responses, On Cue™
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