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): November 15, 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 November 15, 2021, Cue Biopharma, Inc. (the "Company") will be presenting at the Stifel Healthcare Conference. A copy of the Company's corporate presentation to be 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 November 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 hereunto duly authorized.

Cue Biopharma, Inc.

Date: November 15, 2021

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

Exhibit 99.

Corporate Presentation

Immune Responses, On Cue™

Nasdaq: CUE

November 2021

CUE™
BIOPHARMA

Forward-Looking Statements Disclosure

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 the Private Securities Litigation Reform Act of 1995 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, CUE-102 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 and CUE-102, 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.

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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
- Exploit evolutionary selectivity of the immune system enabled by rational protein engineering to design therapeutics with potentially enhanced 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 broad clinical applications

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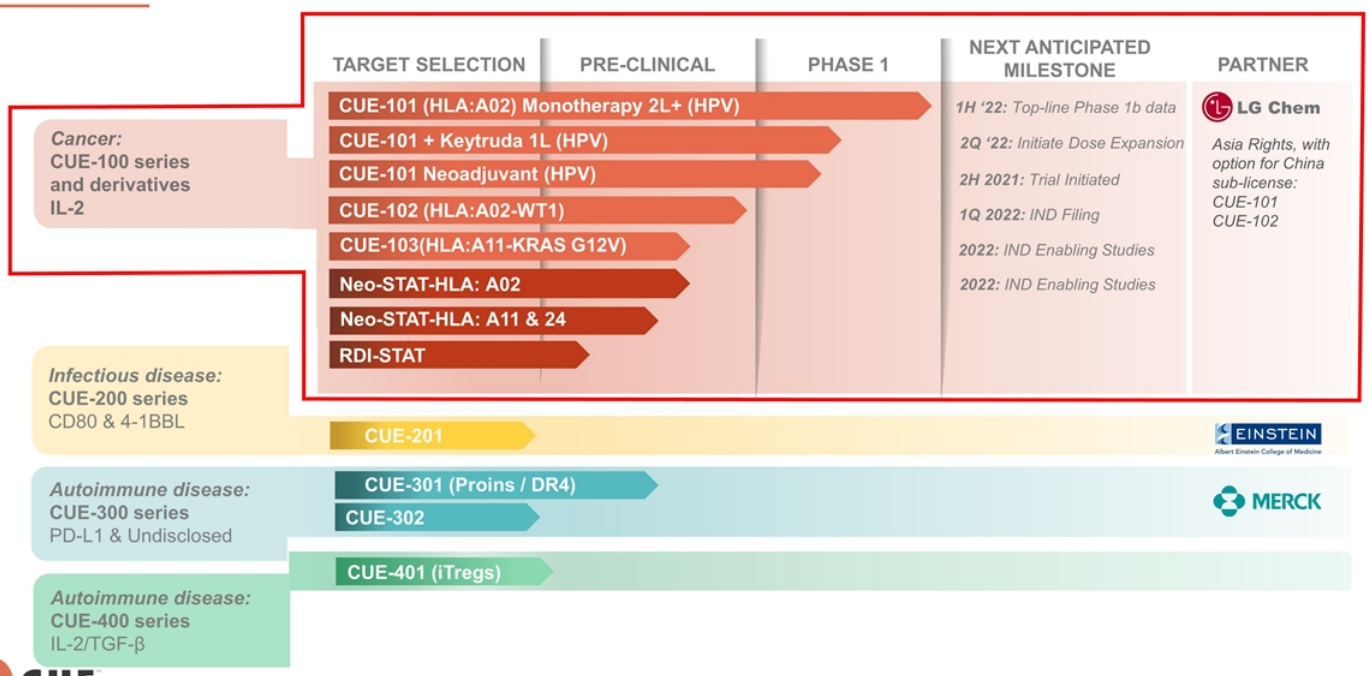
CUE-100 Series: *Changing the Therapeutic Landscape*



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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

A significant challenge in the development of IL-2 as a therapeutic anti-tumor agent is the indiscriminate activation of numerous immune cells – leading to severe toxicity and narrow therapeutic window

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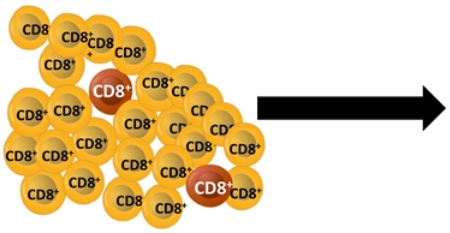
IL-2 Therapy Challenges: Non-selective Immune Activation = Poor Tolerability and Poor Therapeutic Performance

Wild Type IL-2 or IL-2 Variants

Examples

- **Wt IL-2** (aldesleukin)
- **"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.)**

Non-specific Activation of ALL CD8+ T cells

CD8+ TUMOR-SPECIFIC CD8+ T CELL

CD8+ NON TUMOR-SPECIFIC CD8+ T CELL

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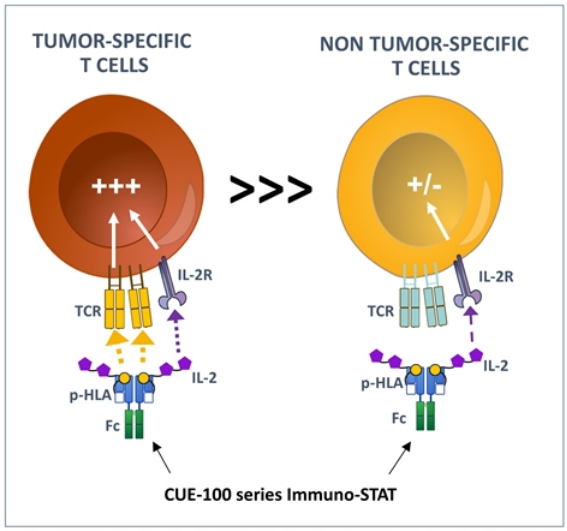
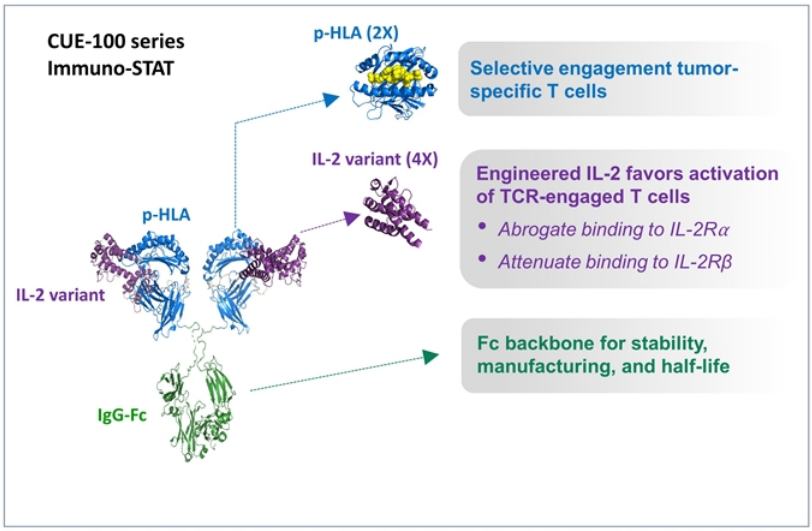
CUE-100 Series: Designing an IL-2 Variant in Context of T Cell Receptor (TCR) Engagement

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





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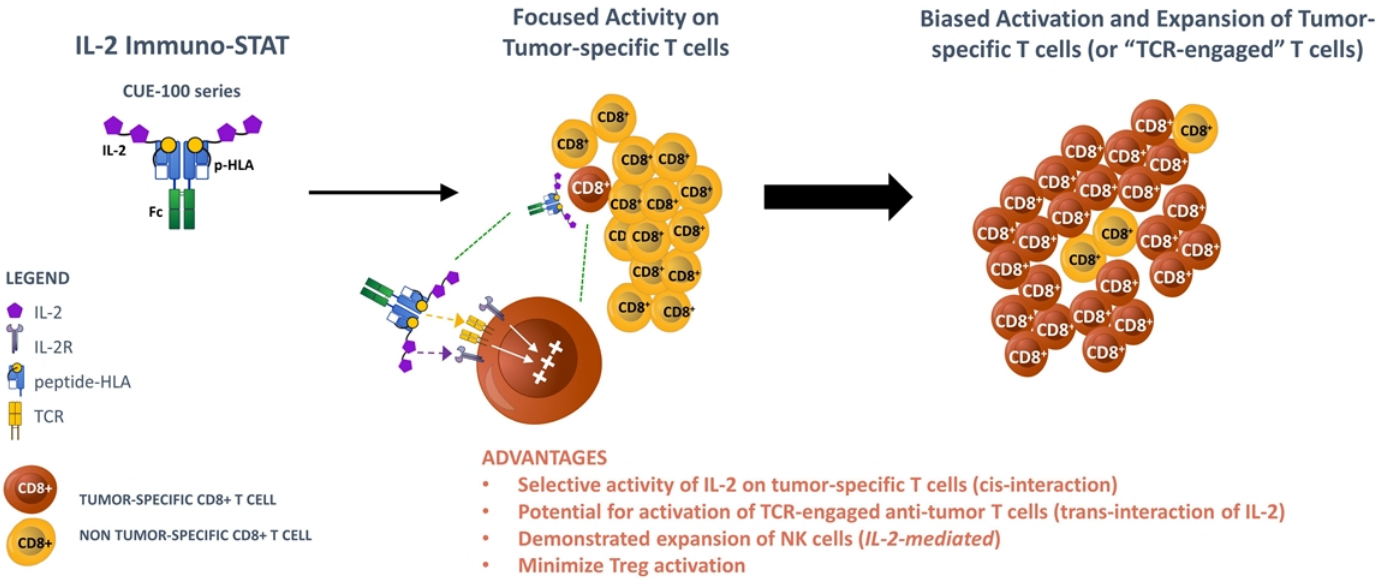
CUE-100 Series: Directing IL-2 Activity to Tumor-specific T cells and Enhancing Tolerability and Efficacy



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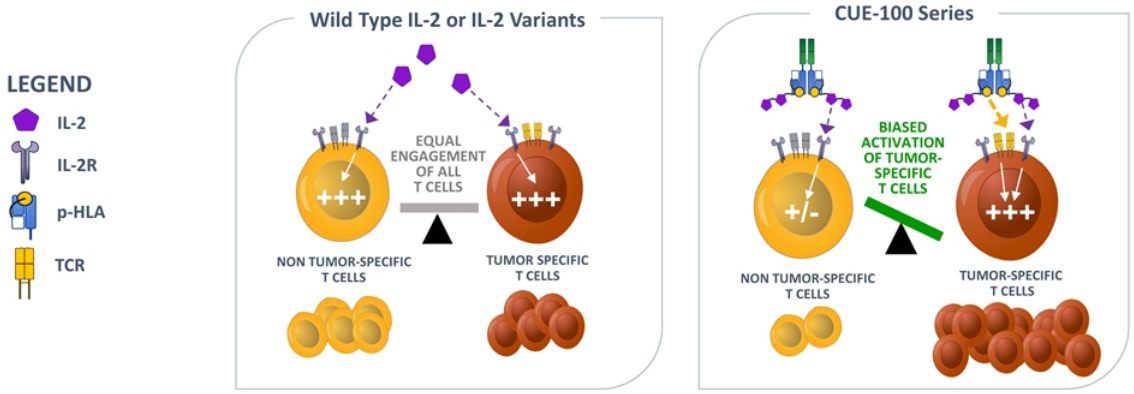
CUE-100 Series: Opportunity to Maximize the Fullest Potential of IL-2

The CUE-100 series has the potential of enabling a broad therapeutic window to enhance IL-2's clinical 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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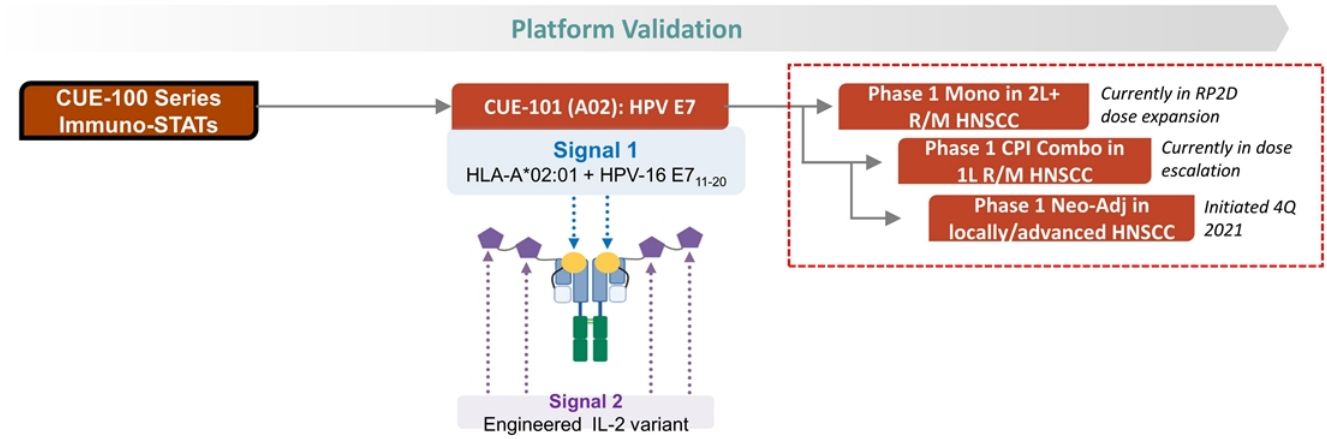
CUE-100 Series: Validate, Expand, and Accelerate



CUE-101 Clinical Data Validates the Immuno-STAT Platform:

- ✓ Clinical and mechanistic PoC for selective IL-2-targeting to tumor-relevant T cells and NK cells
- ✓ Generally well tolerated at efficacious doses
- ✓ PD and PK (lack of evidence of drug-clearing ADAs)
- ✓ Anti-tumor efficacy in monoTx based on RECIST1.1
- ✓ De-risks CUE-101 as well as the IL-2-based CUE-100 series

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

Overview of CUE-101 Phase 1 Monotherapy Dose Escalation and Expansion Study

Phase 1 Part A Dose Escalation Completed and Part B Expansion Enrolling

- 38 patients with recurrent/metastatic H&N cancer across 7 dose escalation cohorts
- 15 patients treated at the RP2D (4 mg/kg)

PK

- Dose proportional exposure, sustained exposure with repeat dosing
- No evidence of anti-drug antibodies (ADAs)

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

Efficacy

- Clinical activity observed across several dose cohorts (partial response/stable disease)
- PR and durable SD observed at RP2D (4.0mg/kg Q3W)

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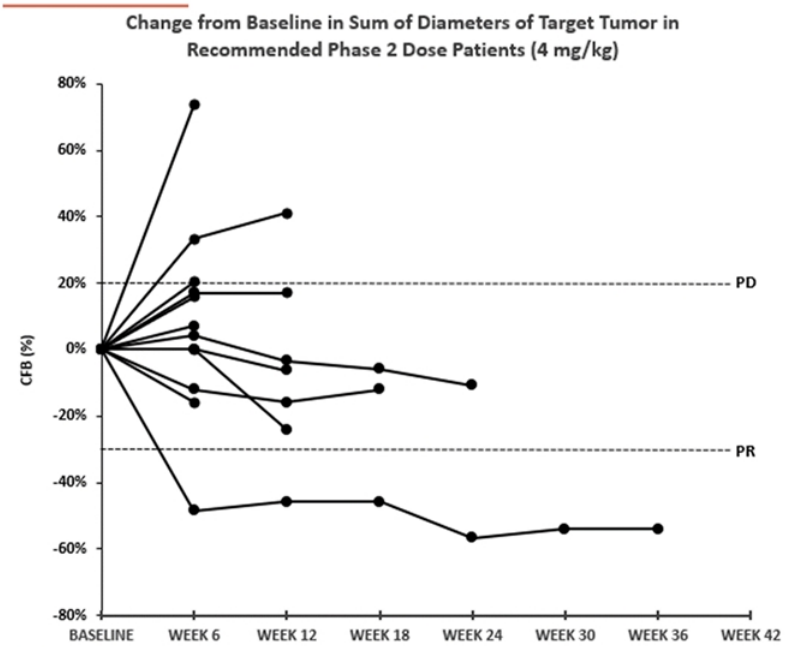
Preliminary Tumor Responses for CUE-101 Monotherapy at the RP2D (4 mg/kg)



Responses	N	%
Objective Response (CR or PR confirmed ≥ 4 weeks)	1	7.7%
Durable Stable Disease (SD sustained for ≥ 12 weeks*)	5	38.5%
Clinical Benefit (CR/PR + durable SD)	6	46.2%

Data extracted from EDC 03-Nov-2021 (7 patients remain on study)
**To qualify as Durable Stable Disease requires SD at ≥2 consecutive post-treatment scans through week 12.*

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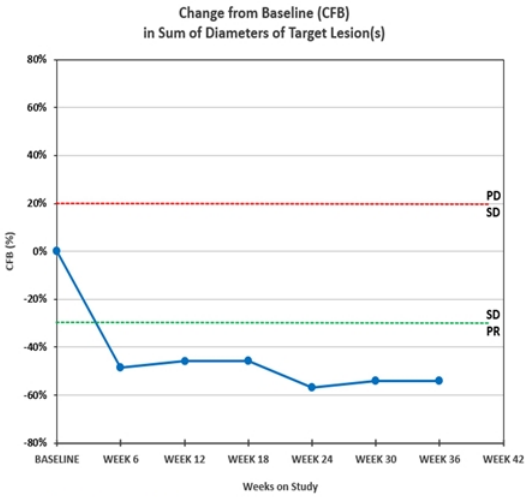
CUE-101: Confirmed PR with ~ 54% Reduction in Target Lesions

Case History

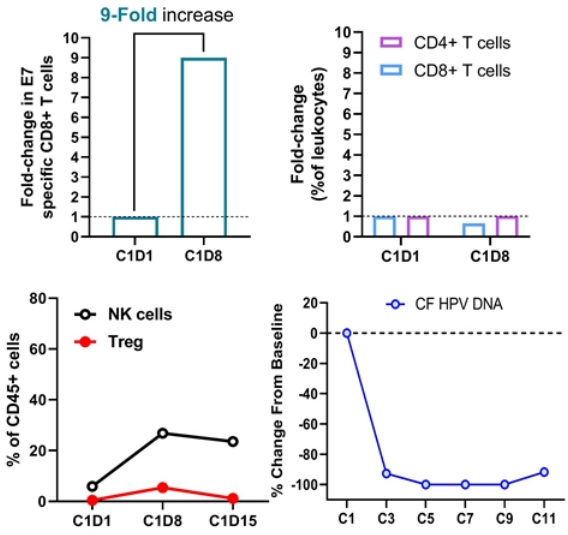
- Prior therapy:
  - 1L cetuximab
  - 2L pembrolizumab
- Progressive disease prior to enrollment
- Treated in metastatic 3L setting with 4.0 mg/kg CUE-101 Q3W (Cohort 6)
- Patient completed 13 cycles of CUE-101 and remains on study with PR ongoing



- Confirmed PR
- Duration of Response 30 weeks
- Patient remains on treatment

**Data updated 28OCT21*

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



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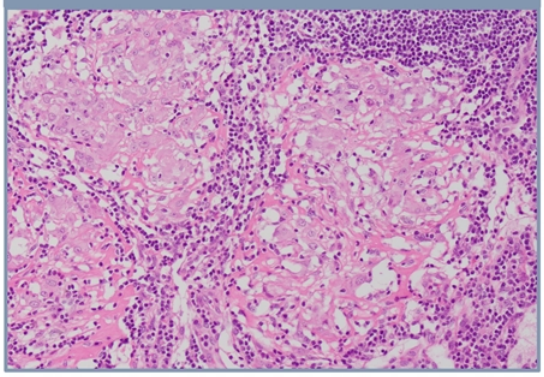
CUE-101: Tumor Necrosis and T Cell Infiltrates in Target Lesions

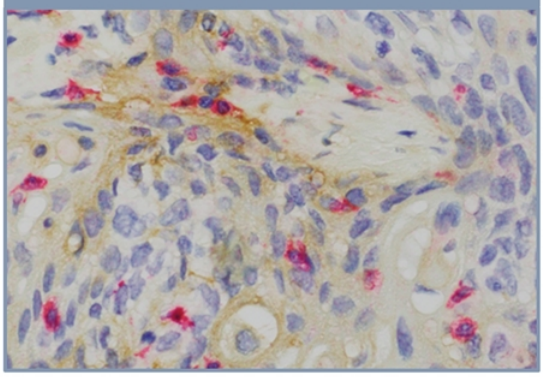
Case History

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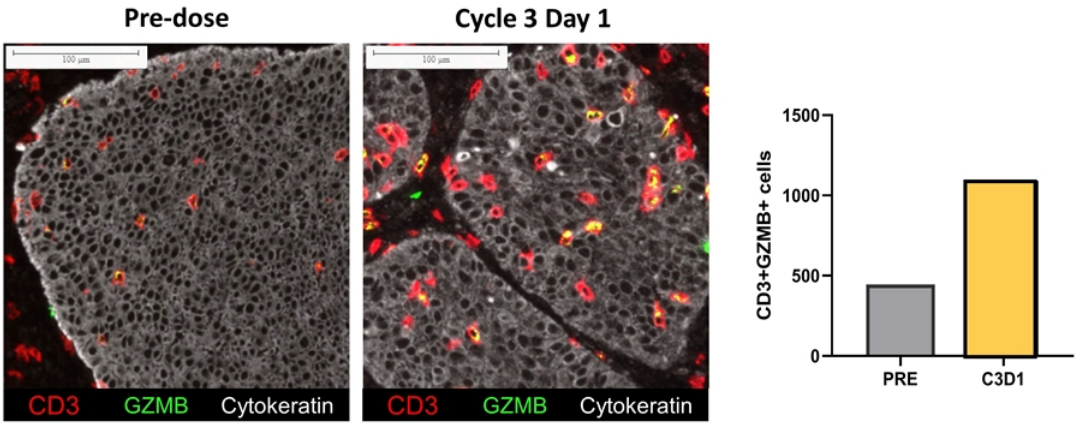
CUE-101: Increase in Tumor Infiltrating T Cells (TILs)

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)



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

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Part C: Dose Escalation of CUE-101 in Combination with Pembrolizumab

Part C: Pembrolizumab Combination Dose Escalation

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

Cohort 3 *Enrolling*

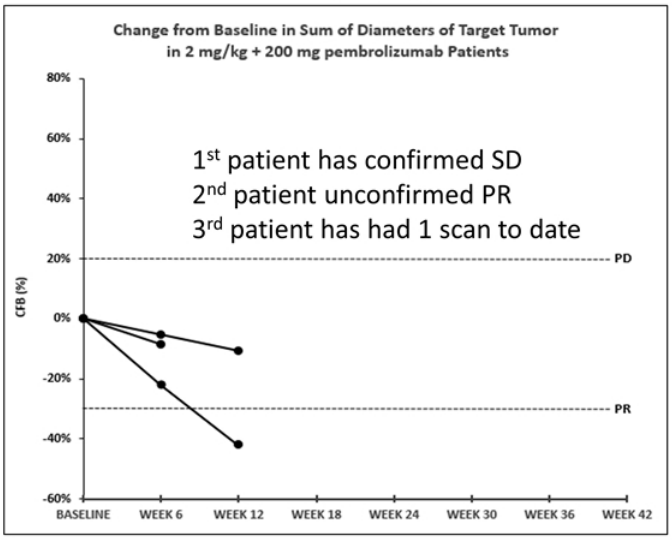
Cohort 2 → *Dosing complete, no DLTs*

Cohort 1 → *Dosing complete, no DLTs*

Preliminary results:

- 3 of 3 patients from cohort 2, 2 mg/kg, demonstrated tumor reductions in their target lesions on their first scan after two cycles of therapy
- All 3 remain on treatment

Cohort 2 (2mg/kg)



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

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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 (study launched in 2H 21)

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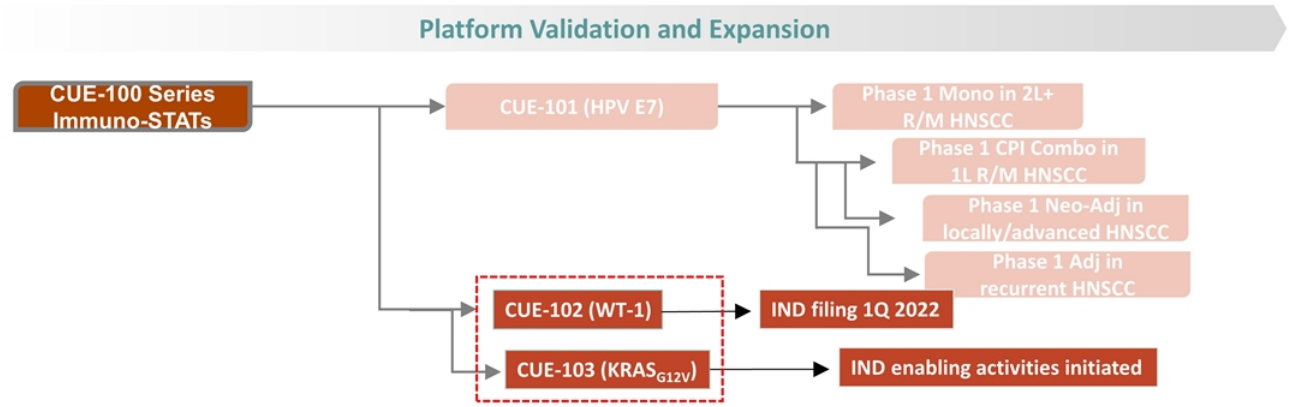
CUE-100 Series: Validate, Expand, and Accelerate



Platform Expansion via CUE-102 and CUE-103:

- ✓ Demonstration of platform modularity
  - ❖ *Expansion of tumor antigens (WT-1, KRAS)*
  - ❖ *Expansion of HLA allelic coverage (A02, A11)*
- ✓ Expansion into major disease indications with significant patient reach
- ✓ Exploits clinical de-risking of IL-2-based CUE-100 series by CUE-101
  - ❖ *Safety and tolerability of IL-2 dosing*
  - ❖ *Well defined regulatory strategy*
  - ❖ *Potential for expedited clinical development path*

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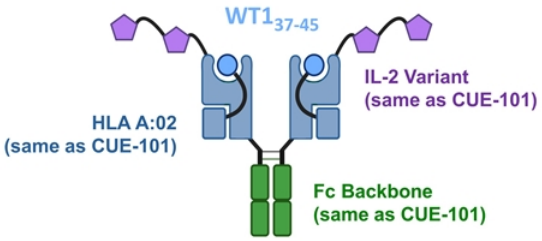
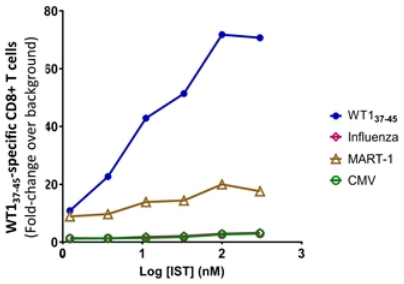
CUE-102: Targeting Wilms Tumor 1 (WT1) – IND Filing 1Q 2022

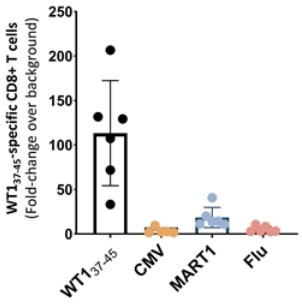
Molecular Design

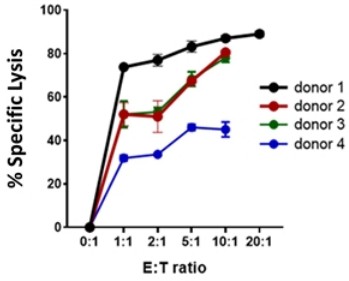


- Top-ranked onco-fetal tumor antigen by the NCI with restricted tissue-expression
- Broad therapeutic opportunity in numerous solid cancers and hematological cancers
- Core IL-2 framework is de-risked by the clinical experience of CUE-101

CUE-102 Selectively Expands WT-1-specific T Cells







CUE-102 Expands WT-1-specific T Cells that are Cytolytic

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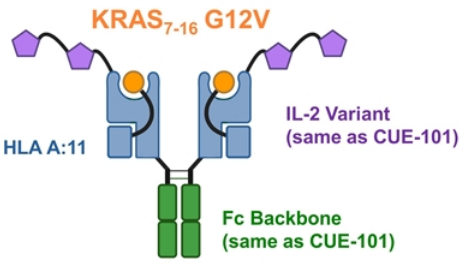
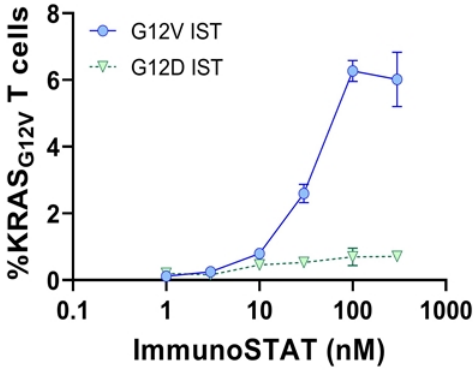
CUE-103: KRAS $_{G12V}$ – Proof of Concept for Targeting KRAS Mutations

Molecular Design



CUE-103 Selectively Expands KRAS$_{G12V}$-specific T Cells



- **Broad therapeutic opportunity for targeting of multiple cancers with KRAS driver mutations (NSCLC, CRC, PC, etc.)**
- **KRAS $_{G12V}$ is a key driver mutation in highly prevalent solid tumors**
- **KRAS$_{G12V}$ is a validated epitope that is recognized by anti-tumor T cells**
- **KRAS$_{G12V}$ A11 asset serves as a beachhead for targeting multiple KRAS mutations (G12D, G12R) and global alleles (i.e., A03, B07) - Source (UPenn PMID 34272369)**

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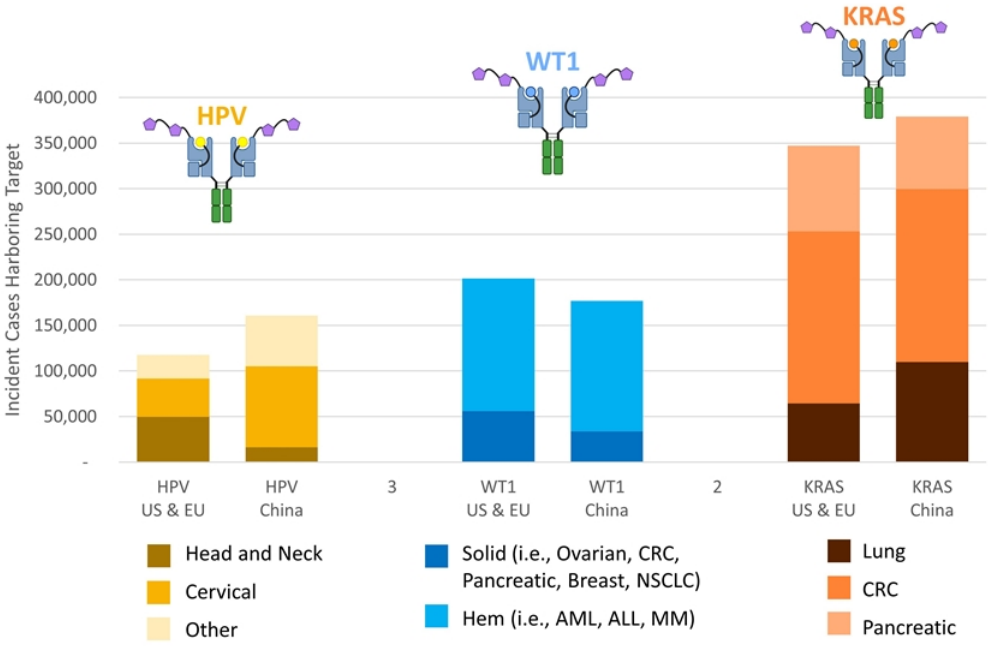
Expansion of Modular CUE-100 Series Into Broad Range of Cancers

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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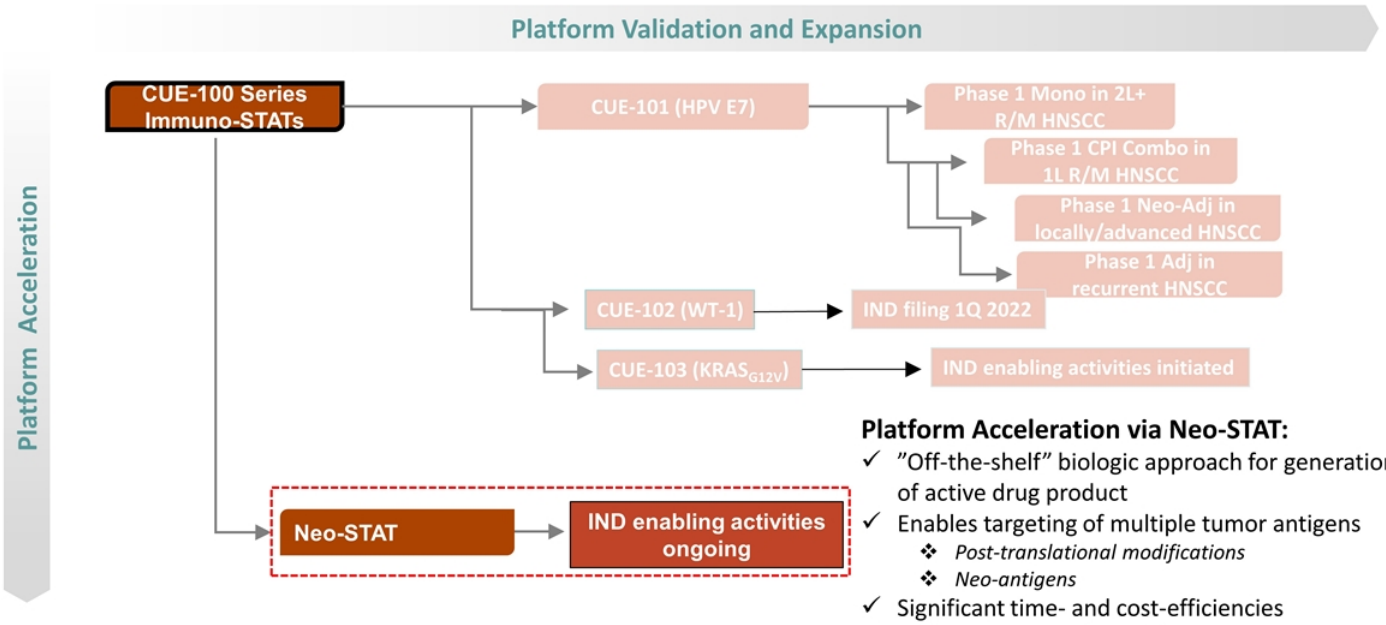
CUE-100 Series: Validate, Expand, and Accelerate



Platform Acceleration via Neo-STAT:

- ✓ "Off-the-shelf" biologic approach for generation of active drug product
- ✓ Enables targeting of multiple tumor antigens
  - ❖ *Post-translational modifications*
  - ❖ *Neo-antigens*
- ✓ Significant time- and cost-efficiencies
- ✓ Exploits the de-risking of the CUE-100 series
  - ❖ *CUE-101, CUE-102, CUE-103*

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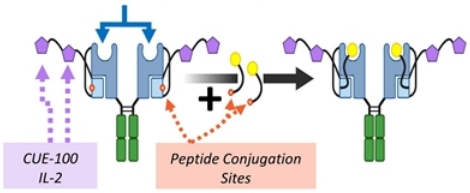
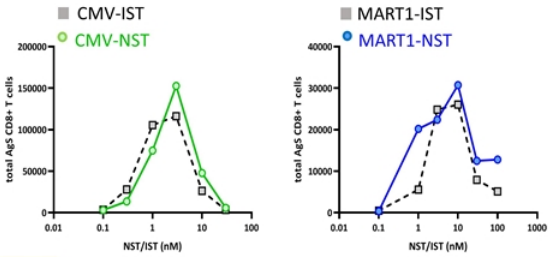
CUE-100 Neo-STAT (NST): "Off-the-Shelf" Universal Scaffold to Address Tumor Heterogeneity and Platform Scalability

Empty HLA
Stabilized through engineering

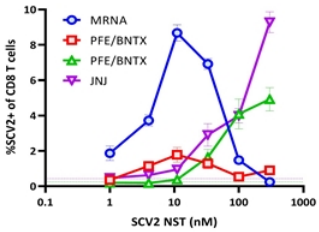
Neo-STAT
Rapid conjugation of tumor epitopes



Neo-STATs (NST) and Immuno-STATs (IST) Exhibit Comparable Activity



NSTs with SARS-CoV2 Epitope Expand CD8+ T Cells from Vaccinated Human Subjects



Neo-STAT Manufacturability	HLA-A02	HLA-A11	HLA-A24
Production	✓✓	✓✓	✓✓
Biophysical Properties	✓✓	✓✓	✓✓
Biological Activity	✓✓	✓✓	Ongoing
Initiation of CMC to support IND	✓✓	Tbd	Tbd

Potential Therapeutic Applications

- Target multiple tumor antigens on multiple HLA alleles
- Peptide mixes / Multi-antigen based cocktail therapy
- Integration of post-translationally modified peptides
- Extension to cancer neoantigens → Personalized medicine

❖ **Neo-STAT will allow for significant time- and cost-efficiencies for rapid generation of therapeutic molecules**

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Summary of Strategic Developments for CUE 100 Series

CUE-101 Clinical Development

- Monotherapy holds promise of registration path for 2L+ HNSCC patients
  - 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 (exploits the potential for synergistic MoA)
- Neoadjuvant study launched 2H (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 human T cell expansion and effector function

CUE-103 targeting KRAS G12V mutation – IND enabling activities ongoing

- 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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