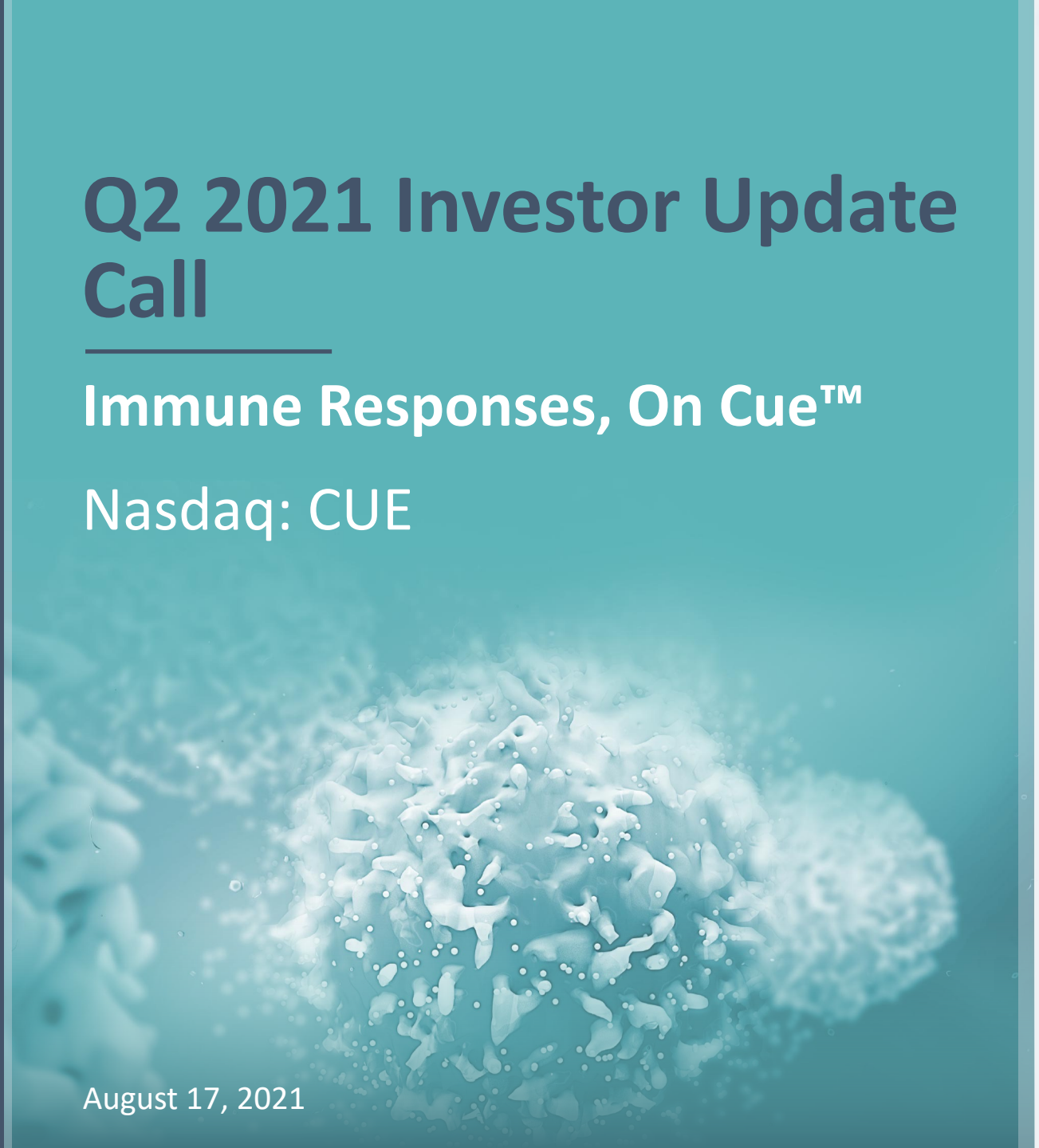
Q2 2021 Investor Update Call

Immune Responses, On Cue™

Nasdaq: CUE



August 17, 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.

Agenda

• **Introduction and 2Q-FY21 Highlights**	Dan Passeri, CEO
• **IL-2-based CUE-100 series**	Anish Suri, President and CSO
• **CUE-101 Clinical Update**	Dr. Ken Pienta, Acting CMO Dr. Matteo Levisetti, SVP, Clinical Development
• **Pipeline Progress**	Anish Suri, President and CSO
• **2Q-FY21 Financial Results & Guidance**	Kerri-Ann Millar, CFO
• **Concluding Remarks**	Dan Passeri, CEO
• **Q&A**	All

CUE BIOPHARMA

Cue Biopharma's Vision

Leading the next wave of disruptive, breakthrough immuno-therapies 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
- Enabled by rational protein engineering to design therapeutics with potentially enhanced selectivity and activity
- Emerging clinical data, including clinical response and patient benefit, provides potential for de-risking and validation of the ***entire*** platform
- Platform modularity and scalability expected to support versatile clinical applications and enhanced efficiencies in manufacturing and cost

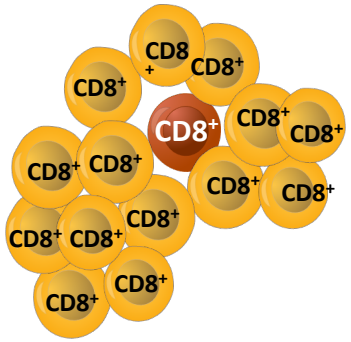
Interleukin-2 (IL-2): A Proven Therapy, but with Significant Limitations and Liabilities

- **IL-2 is an approved immuno-therapy for melanoma and renal cell carcinoma (RCC)**
- **Lack of selectivity and safety of IL-2 treatment have precluded its fullest potential in cancer immunotherapy**
  - *E.g., vascular-leak syndrome (VLS), cytokine-release syndrome (CRS)*
  - *E.g., systemic activation of T cells, including Tregs*
- **Opportunity for next-gen breakthrough IL-2 therapies to address**
  - *Selectivity and activity (focus on tumor-specific immune cells)*
  - *Safety and tolerability (avoid VLS, CRS, systemic activation of T cells)*

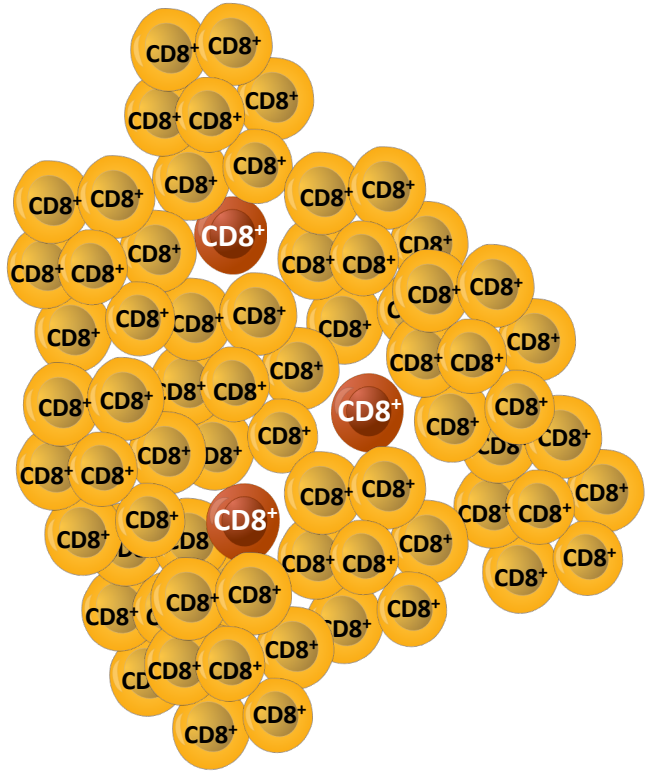
IL-2 Therapy Challenges: Non-selective T cell Activation = Poor Tolerability and Poor Therapeutic Performance as Monotherapy

Wild Type IL-2 or IL-2 Variants

Lack of Selectivity for Tumor-specific CD8+ T cells



Non-specific Activation of ALL CD8+ T cells



CD8+ TUMOR-SPECIFIC CD8+ T CELL

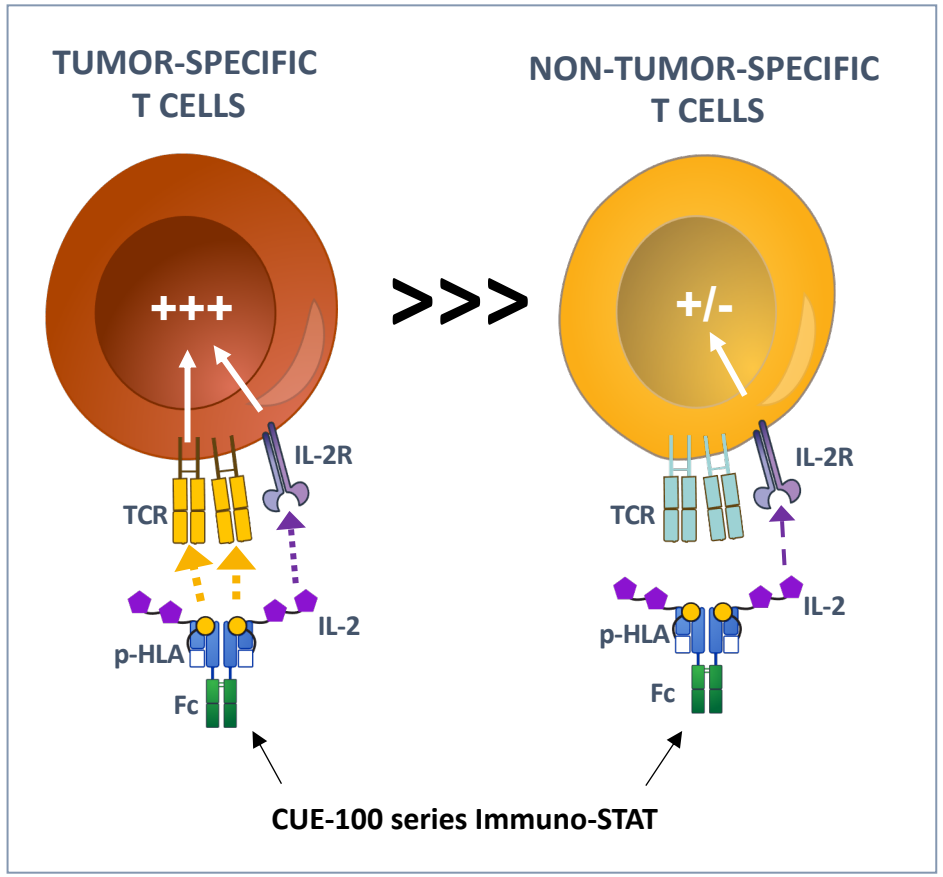
CD8+ NON TUMOR-SPECIFIC CD8+ T CELL

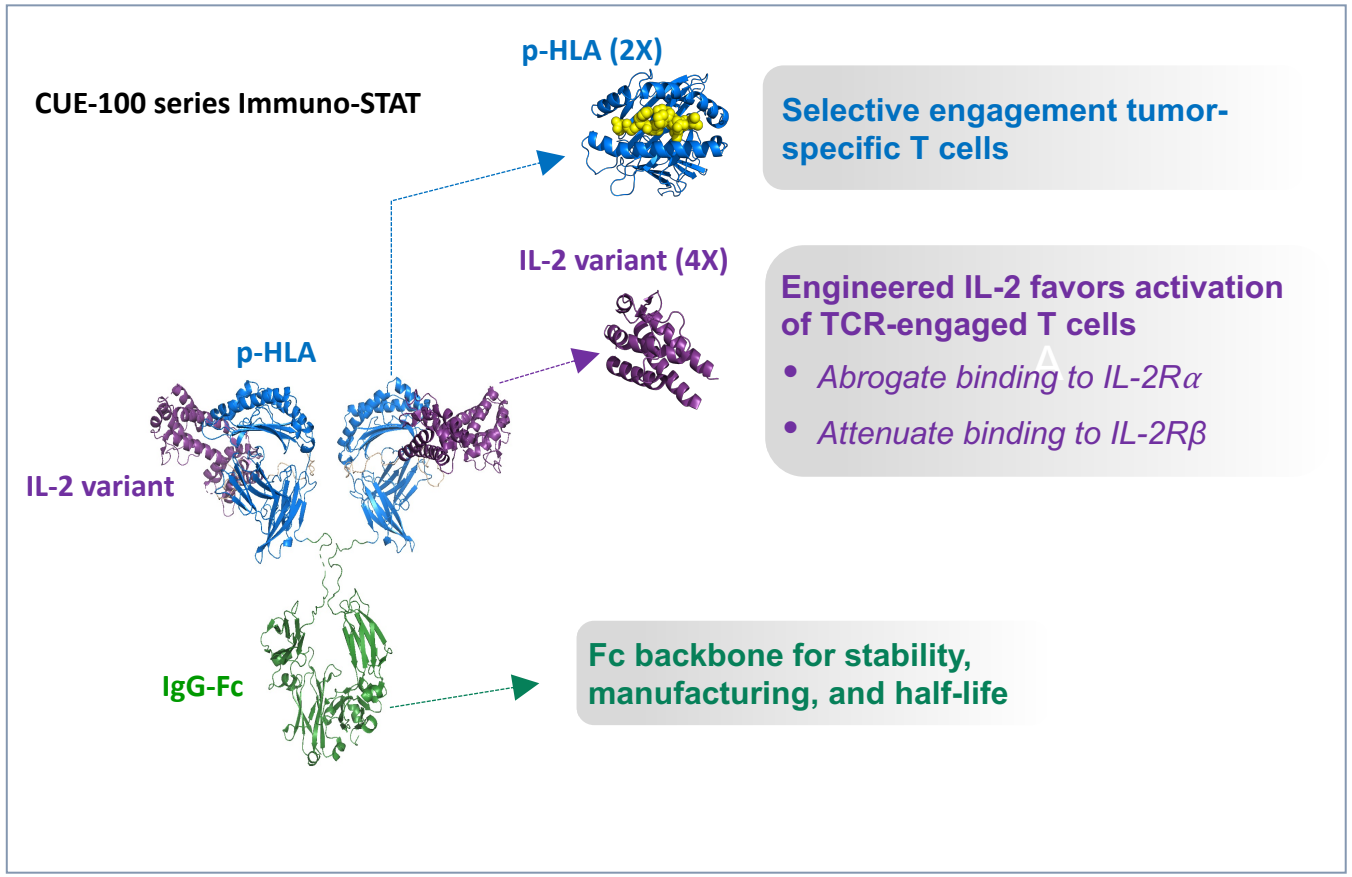
CHALLENGES

- Lack of selectivity for tumor-specific T cells
- Activation of Tregs
- Toxicities (VLS, CRS etc.)

CUE-100 Series: Designing an IL-2 Variant in Context of TCR Engagement

Molecular structure exploits TCR and IL-2 engagement to tune optimal signal amplitude for CD8+ T cell activation

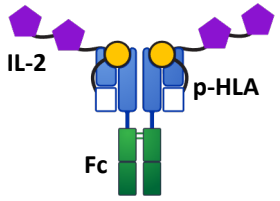




CUE-100 Series: Preferential Activity of IL-2 on Tumor-specific T cells

IL-2 Immuno-STAT

CUE-100 series



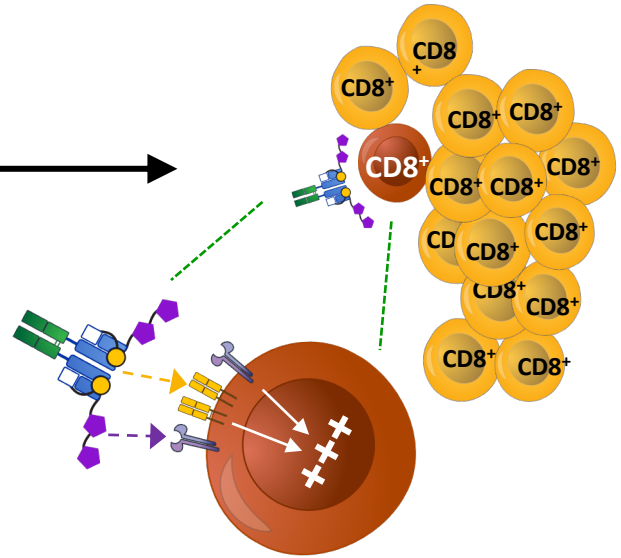
LEGEND

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

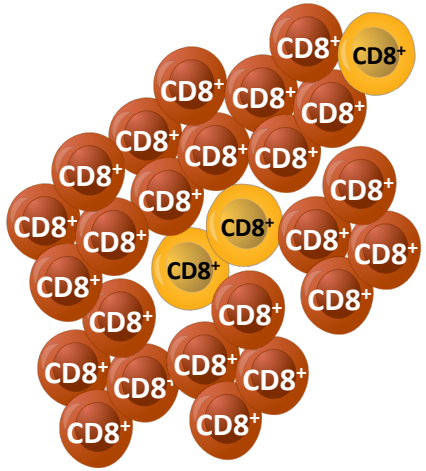
CD8+ TUMOR-SPECIFIC CD8+ T CELL

CD8+ NON TUMOR-SPECIFIC CD8+ T CELL

Focused Activity on Tumor-specific T cells



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



ADVANTAGES

- Selective activity of IL-2 on tumor-specific T cells (cis-interaction)
- Potential for activation of TCR-engaged anti-tumor T cells (trans-interaction of IL-2)
- Demonstrated expansion of NK cells (*IL-2-mediated*)
- Minimize Treg activation
- Generally well-tolerated to date

  lead candidate CUE-101 dosed up to 8.0 mg/kg with no MTD

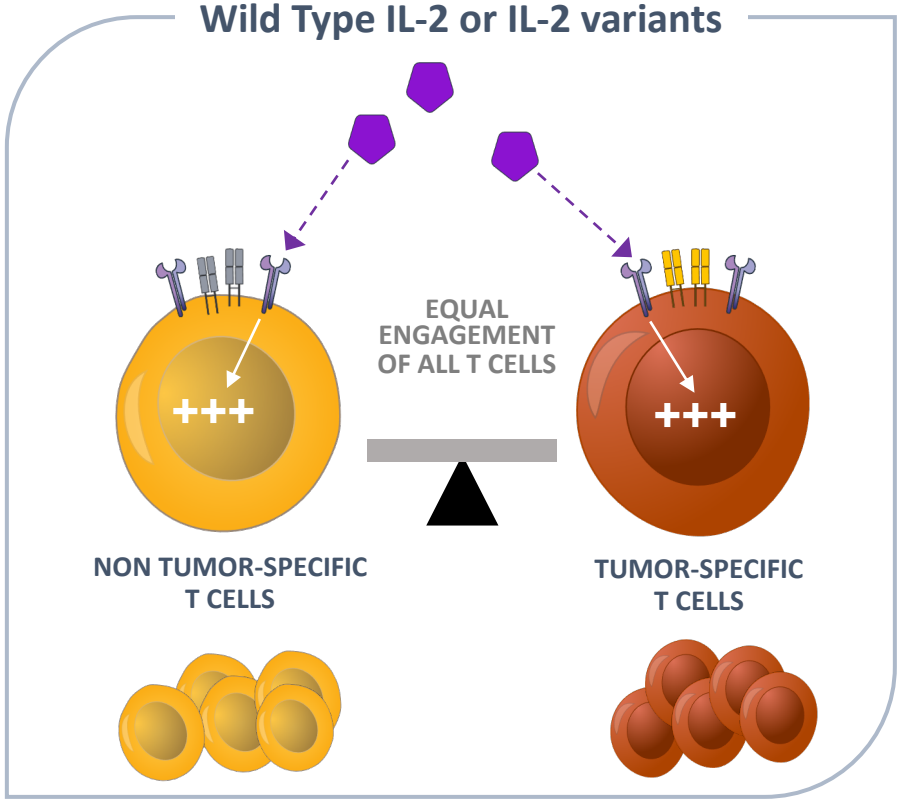
CUE-100 Series: Opportunity to Maximize the Fullest Potential of IL-2

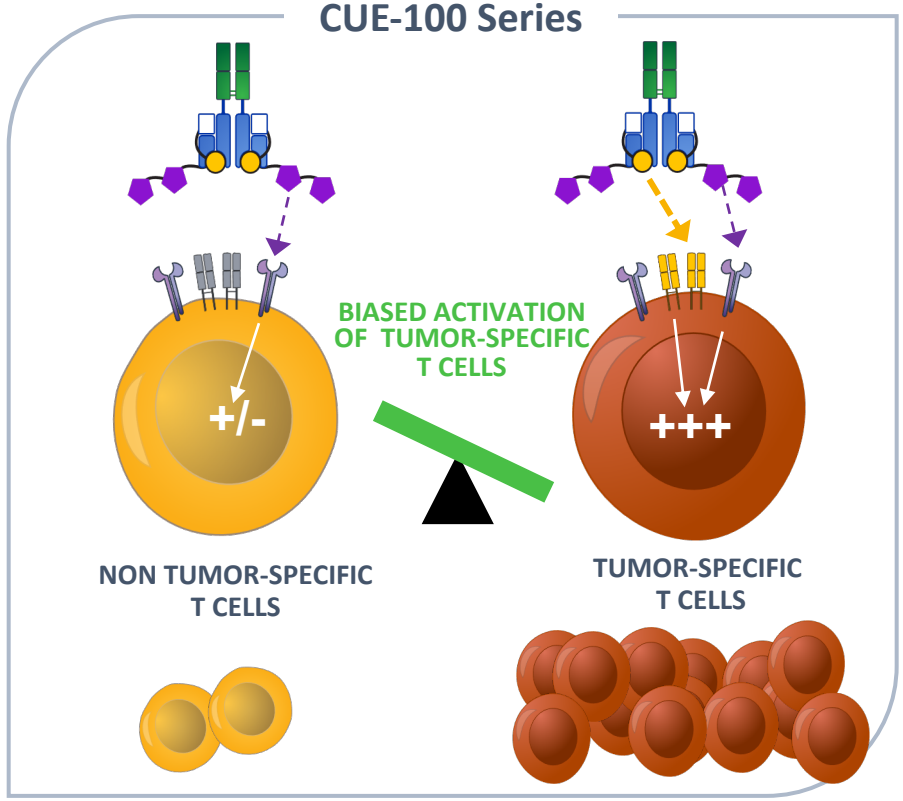
IL-2

IL-2R

p-HLA

TCR





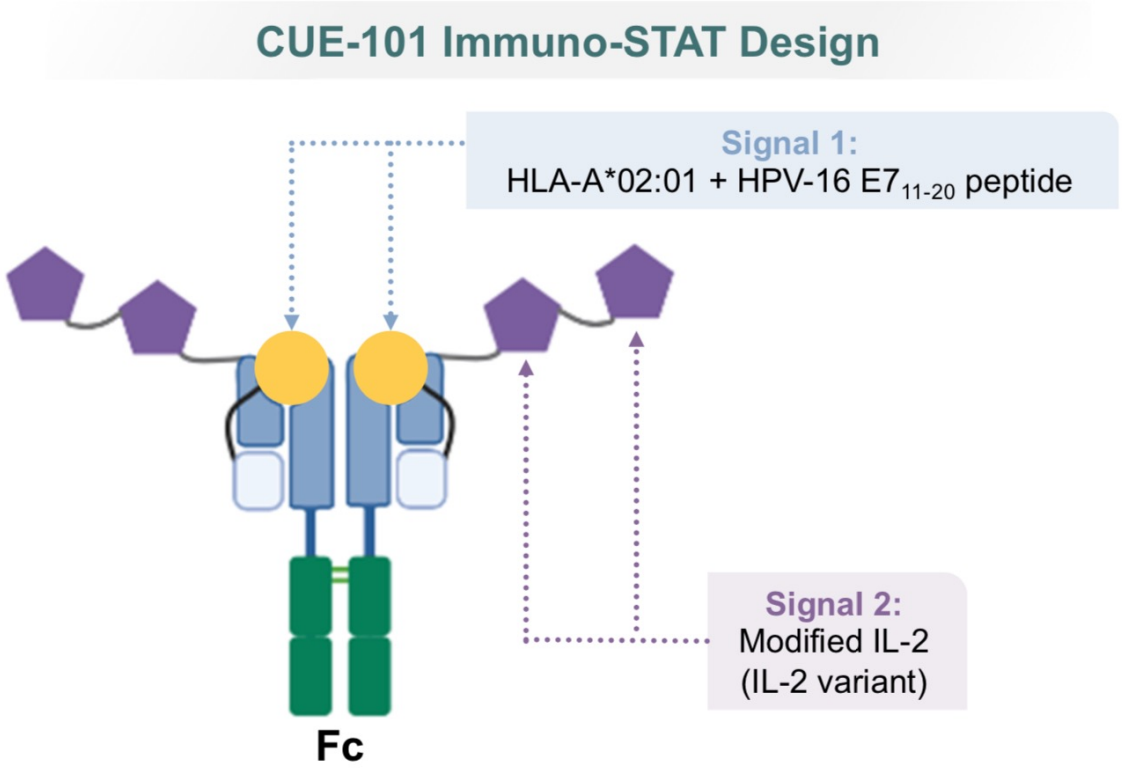
TOLERATED DOSES:

- Aldesleukin: 0.037 mg/kg (approved dose)
- NKTR-214 and ALKS-4230: 0.006 mg/kg (RP2D)
- THOR-707: 0.006 to 0.024 mg/kg

CUE-101: dosed up to 8.0 mg/kg
NO MTD identified

CUE BIOPHARMA

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



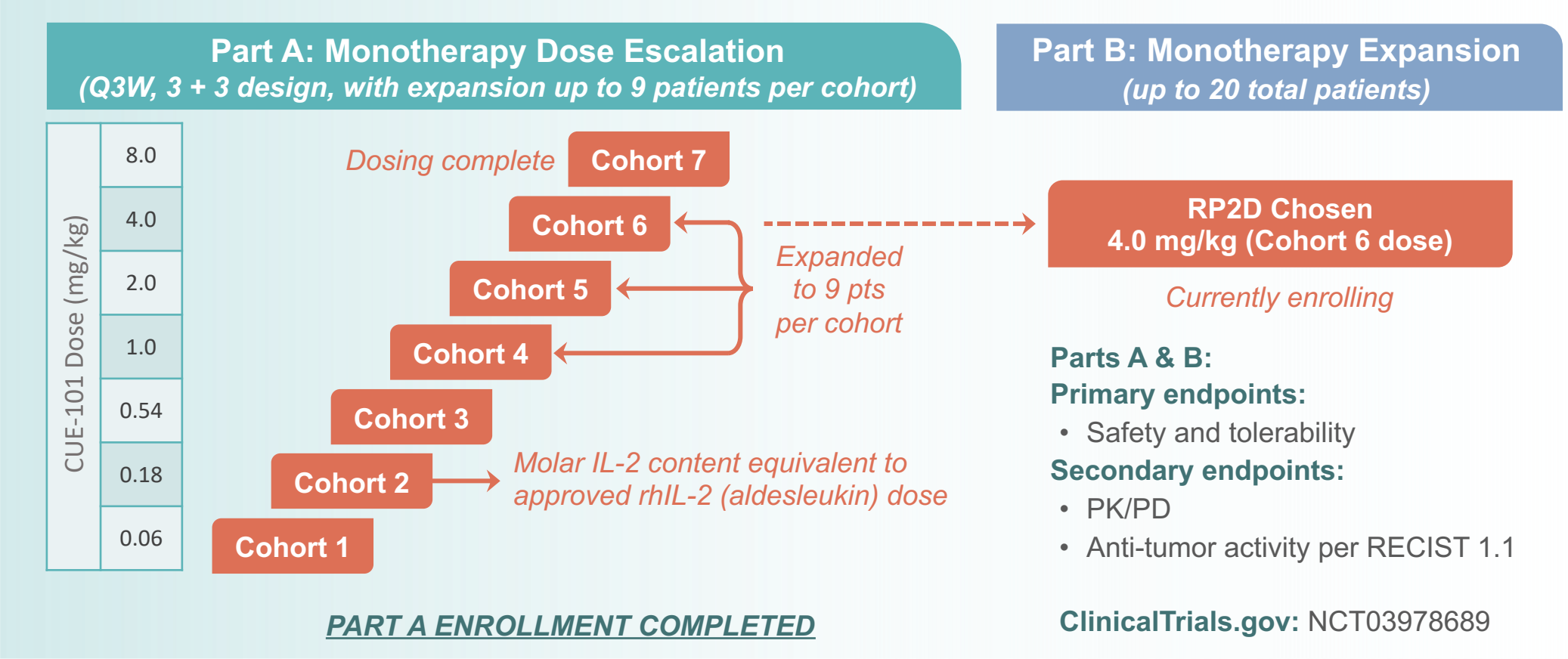
Clinical Rationale

- 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: Ongoing Monotherapy First-in-Human Phase 1 Trial

No maximal tolerated dose (MTD) observed in patients dosed up to 8 mg/kg



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: Lead Clinical-Stage Asset from IL-2 Based CUE-100 Series

Cohort 6 dose (4.0mg/kg Q3W) selected as RP2D with dose expansion ongoing

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

Enrollment

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

Efficacy

- 1 confirmed PR and 8 confirmed SD
- Clinical Benefit Rate of >25% in first 33 patients treated

PD

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

Safety

- Generally well-tolerated with no MTD

CUE-101-01: Patient Characteristics of CUE-101 Monotherapy (N=39)

Age (years)	Mean (range)	63.8 (48-82)
Sex	Male	38 (97.4%)
	Female	1 (2.6%)
ECOG	0	17 (43.6)
	1	22 (56.4)
Prior Lines of Therapy*	Median (range)	3 (1-6)
	• Platinum Based	35 (89.7%)
	• Checkpoint Inhibitor	36 (92.3%)
	○ PD-1	33 (84.6%)
	▪ Nivolumab	16 (41.0%)
	▪ Pembrolizumab	19 (48.7%)
	○ PD-L1	6 (15.4%)
	○ CTLA-4	1 (2.6%)
	• TK Inhibitor	2 (5.1%)
	• EGFR Inhibitor	27 (69.2%)

*Data cut-off 27 Jul 21: All patients are HLA-A*201-positive and HPV16-positive.*
**Patients reporting > 1 prior line of therapy are counted once per category and may be included in > 1 category.*

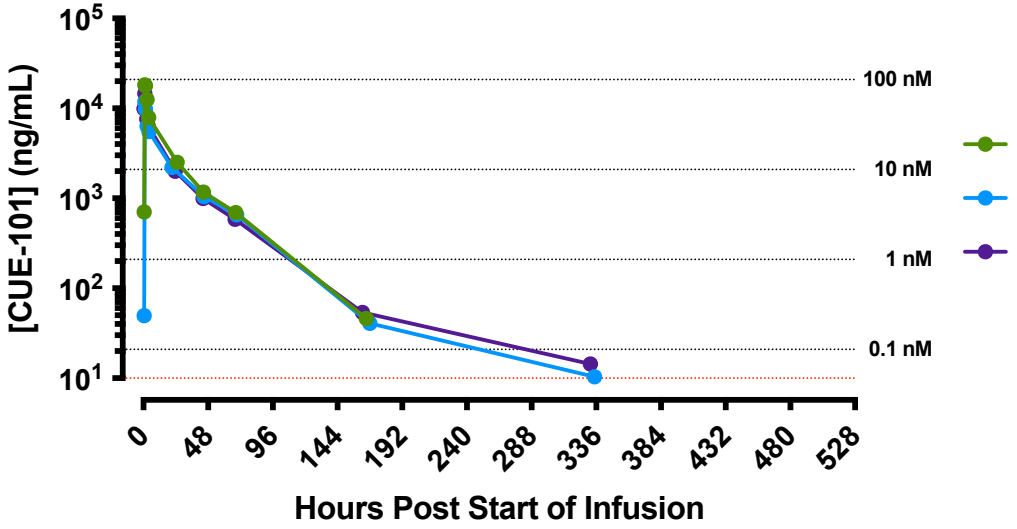
CUE-101-01: Treatment Emergent Adverse Events

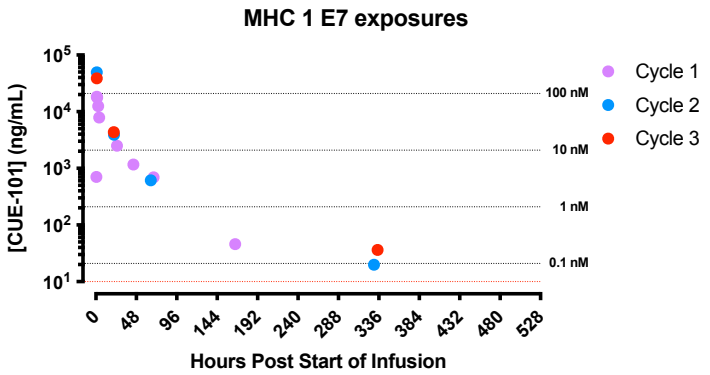
	Treatment Related Adverse Events (N=42)		All Adverse Events (N=42)	
Preferred Term	**≥ Grade 3**	**All Grades**	**≥ Grade 3**	**All Grades**
Overall Frequency	**9 (21.4%%)**	**28 (66.7%%)**	**18 (42.9%%)**	**34 (81.0%%)**
Fatigue	2 (4.8%)	12 (28.6%)	2 (4.8%)	17 (40.5%)
Anaemia	1 (2.4%)	2 (4.8%)	2 (4.8%)	13 (31.0%)
Lymphocyte count decreased	3 (7.1%)	3 (7.1%)	6 (14.3%)	10 (23.8%)
Chills	0 (0.0%)	7 (16.7%)	0 (0.0%)	9 (21.4%)
Decreased appetite	0 (0.0%)	3 (7.1%)	3 (7.1%)	8 (19.0%)
Dyspnoea	0 (0.0%)	1 (2.4%)	1 (2.4%)	7 (16.7%)
Cough	0 (0.0%)	2 (4.8%)	0 (0.0%)	6 (14.3%)
Dysphagia	0 (0.0%)	0 (0.0%)	1 (2.4%)	6 (14.3%)
Hyponatraemia	0 (0.0%)	1 (2.4%)	0 (0.0%)	6 (14.3%)
Hypophosphataemia	0 (0.0%)	3 (7.1%)	1 (2.4%)	6 (14.3%)
Muscular weakness	0 (0.0%)	4 (9.5%)	0 (0.0%)	6 (14.3%)
Nausea	1 (2.4%)	6 (14.3%)	1 (2.4%)	6 (14.3%)
Weight decreased	0 (0.0%)	2 (4.8%)	0 (0.0%)	6 (14.3%)
Arthralgia	0 (0.0%)	3 (7.1%)	0 (0.0%)	5 (11.9%)
Blood lactate dehydrogenase increased	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (11.9%)
Diarrhoea	1 (2.4%)	3 (7.1%)	1 (2.4%)	5 (11.9%)
Myalgia	0 (0.0%)	5 (11.9%)	0 (0.0%)	5 (11.9%)
Rash maculo-papular	1 (2.4%)	4 (9.5%)	1 (2.4%)	5 (11.9%)

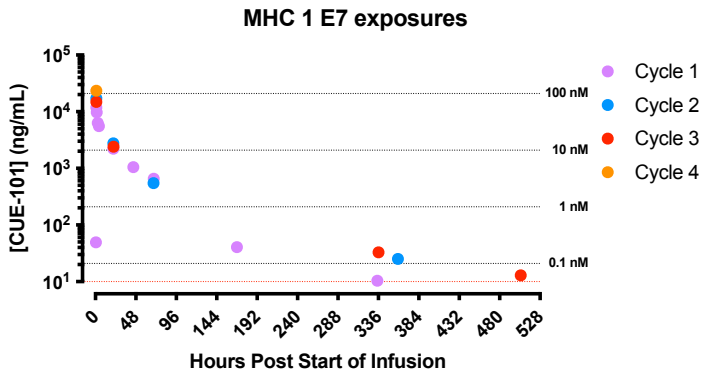
Data cut-off 01 Jul 21

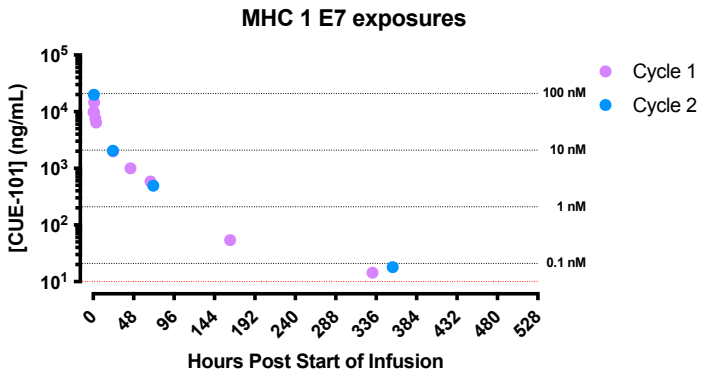
AEs are coded using MedDRA V21.0 and NCI-CTCAE v5.0. At each level of summation patients reporting > 1 occurrence of the same AE are counted only once at the highest toxicity. Treatment-relatedness is assessed by the investigator as 'Definitely', 'Probably', or 'Possibly' related to CUE-101 and/or Pembrolizumab. ***Treatment related SAEs (all ≤ 5% frequency):*** *Anemia, diarrhea, nausea, vomiting, fatigue, infusion related reaction, dehydration, hyponatraemia, acute kidney injury, pemphigoid, vertigo, pneumonitis*

Cohort 6 (4mg/kg) PK: Low Inter-Patient Variability and Sustained Exposure with Repeat Dosing



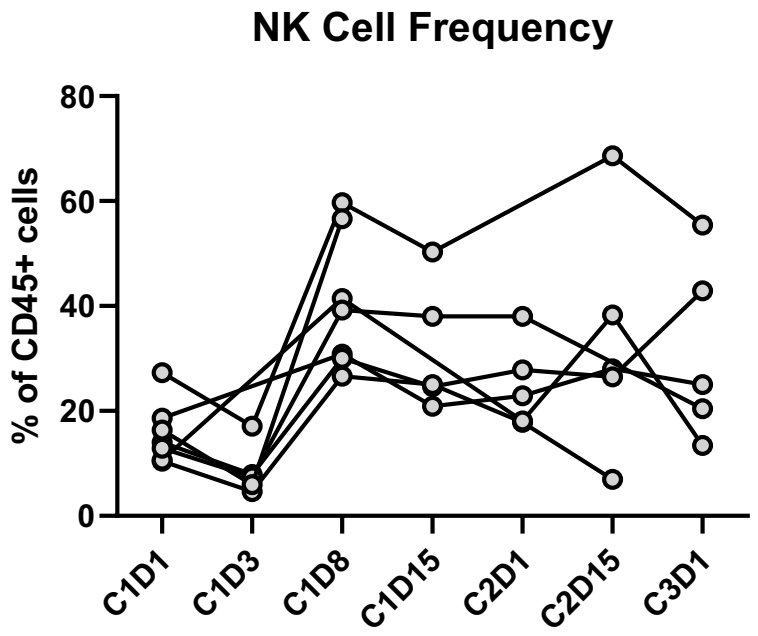




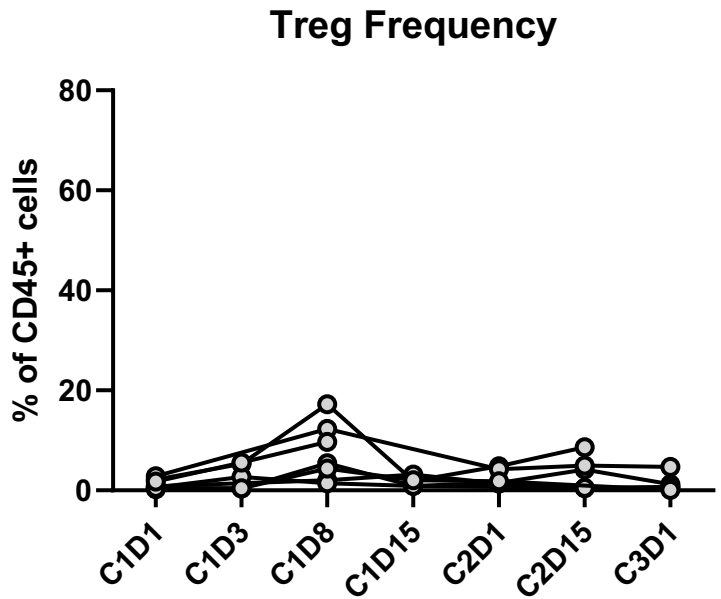


PD Data from Cohort 6: Underscores the Rational Design and Mechanistic Activity of CUE-101

Notable increase in NK cells post dosing with CUE-101



Transient increase in CD4+ Foxp3+ T cells post dosing with CUE-101

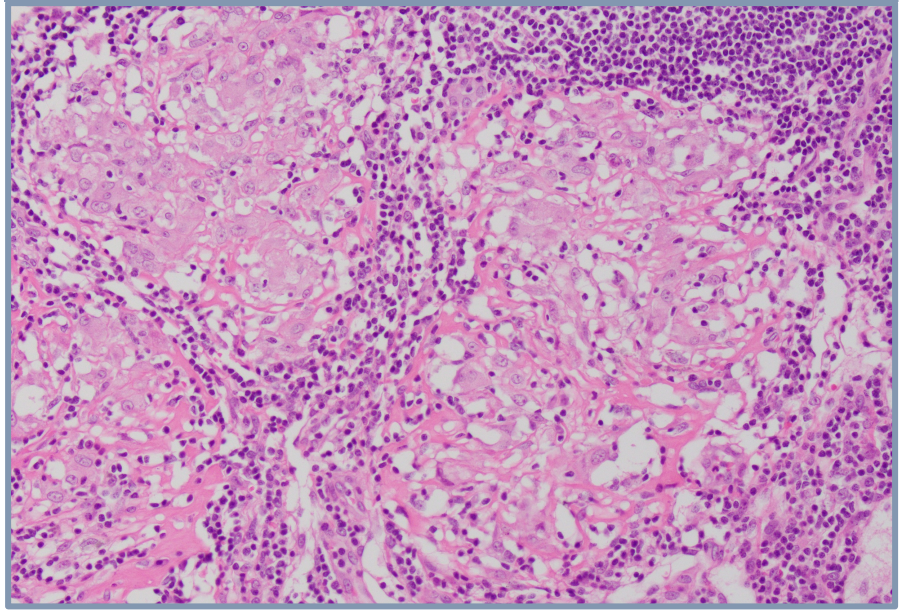


CUE-101: Tumor Necrosis and T Cell Infiltrates in Target Lesions

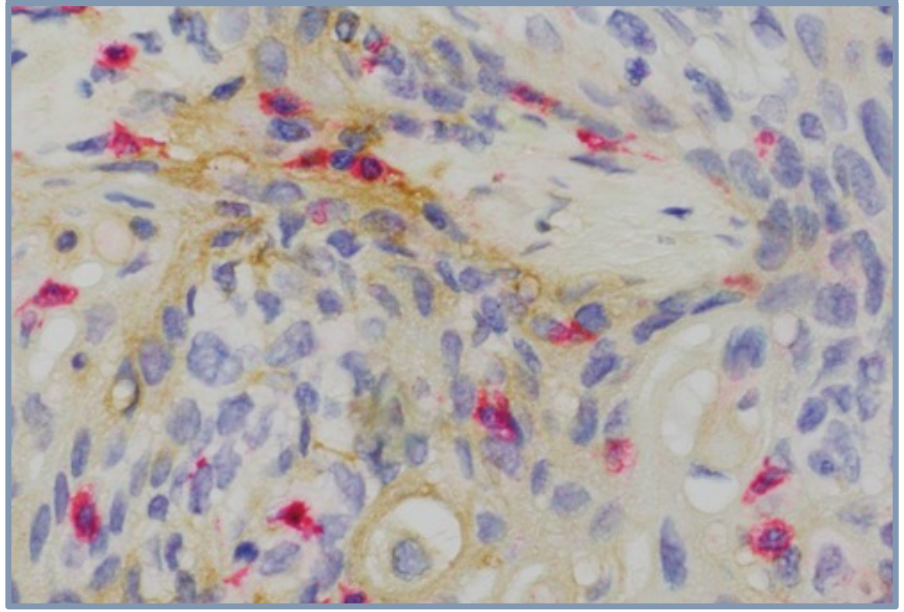
Case History

- **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)



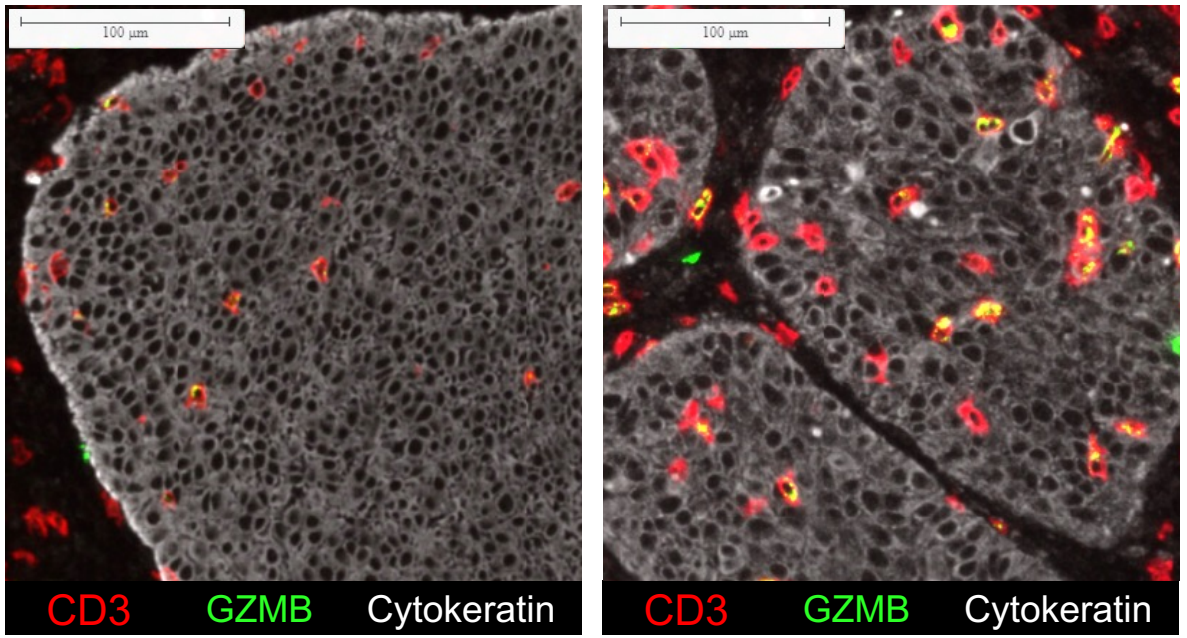
Patient remains disease free post resection

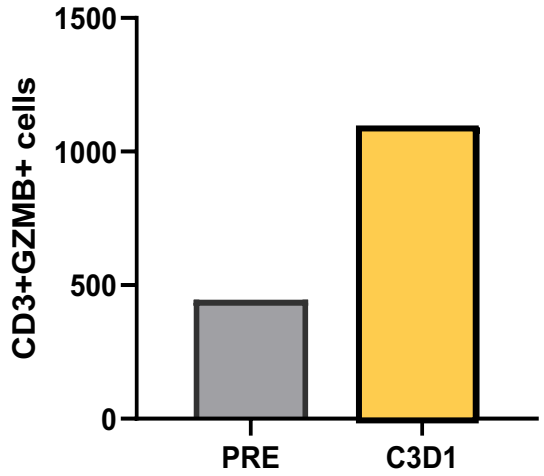
CUE-101: Increase in Tumor Infiltrating T Cells (TILs)

Case History

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

Pre-dose | **Cycle 3 Day 1**



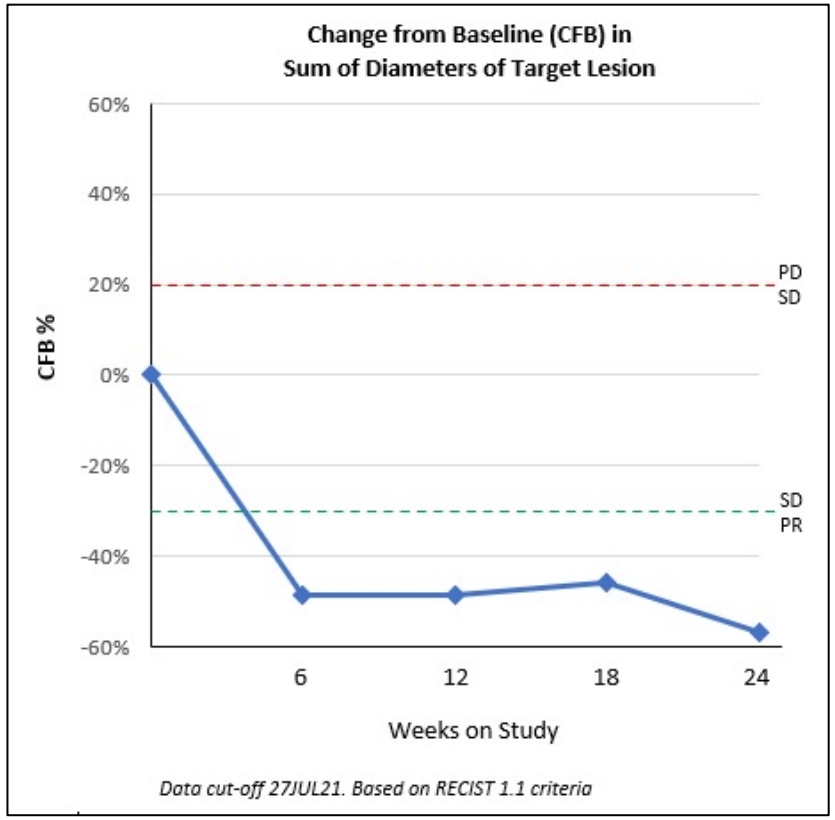


IHC staining indicates increase in TILs (CD3+) and granzyme (GZMB) within a target tumor lesion following CUE-101 monotherapy

CUE-101: Confirmed PR with ~ 57% Reduction in Target Lesions

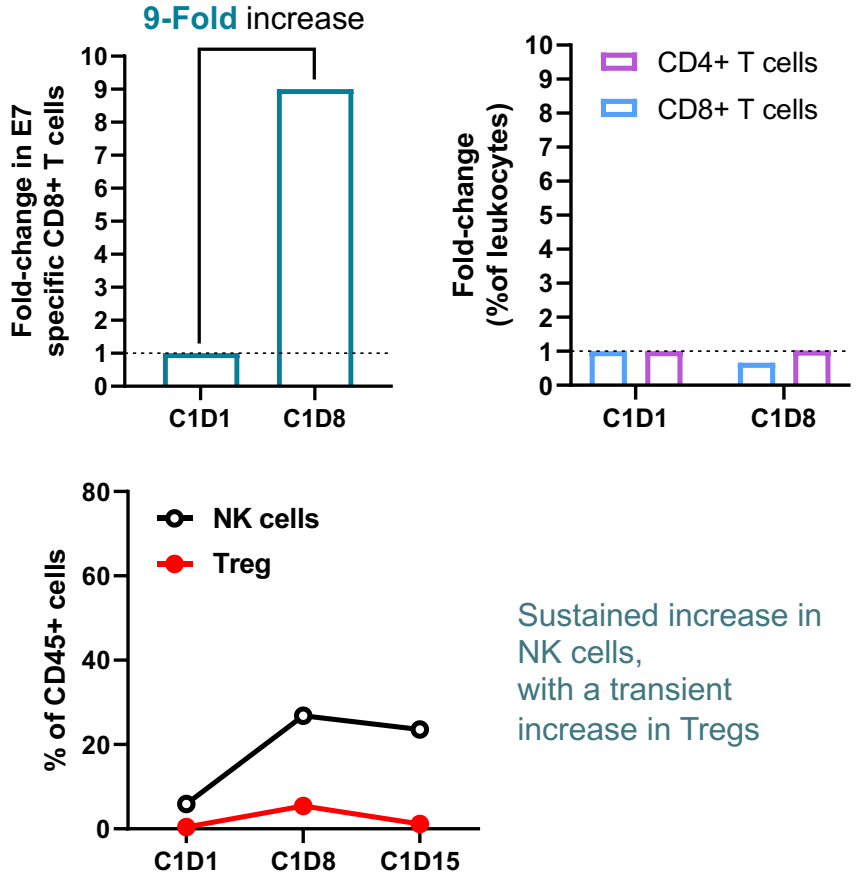
Case History

- **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 9 cycles of CUE-101 and remains on study with PR ongoing**



- Confirmed PR
- Duration of Response 18 weeks
- Patient remains on treatment

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

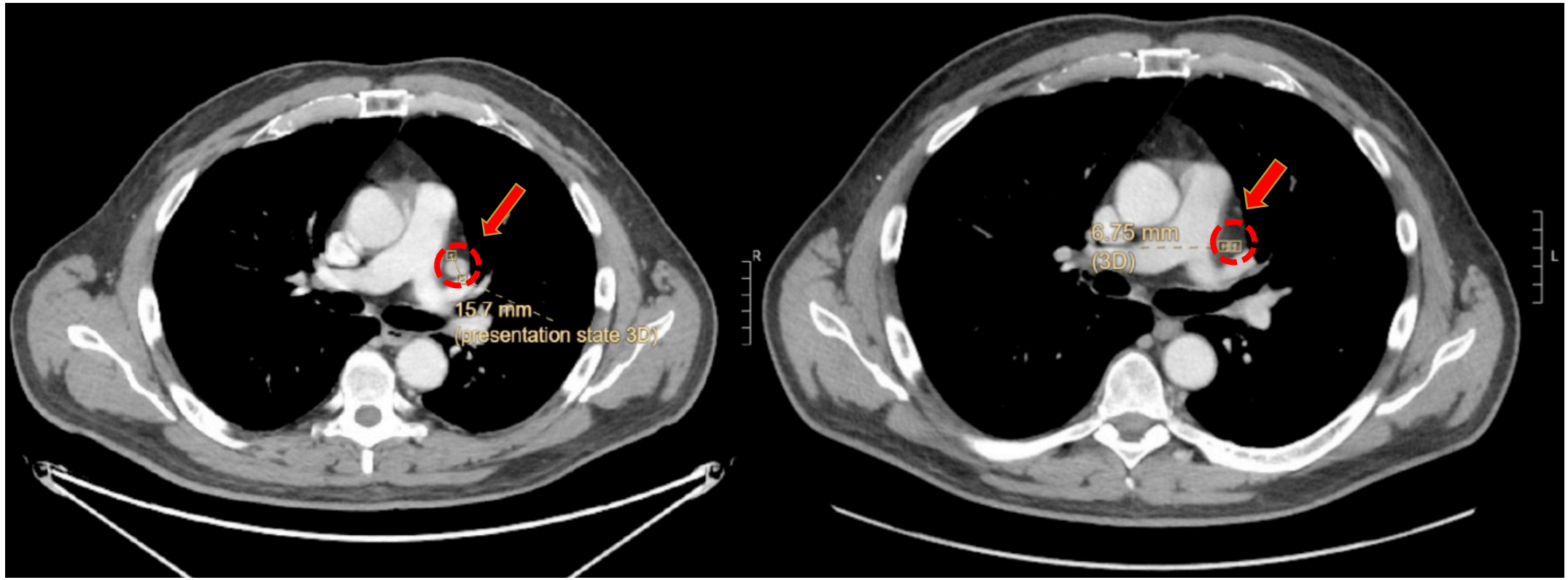


Sustained increase in NK cells, with a transient increase in Tregs

Confirmed PR in Patient Treated at RP2D

FEB 2021

JUN 2021



~57% reduction in left hilar lesion

CUE-101: Multiple Shots on Goal for Potential Registration Paths

Monotherapy

- 3rd line therapy for HPV+ head and neck cancer
- Potential option for 2nd line therapy in CPS <1 patients who are not eligible for pembrolizumab

Combination therapy

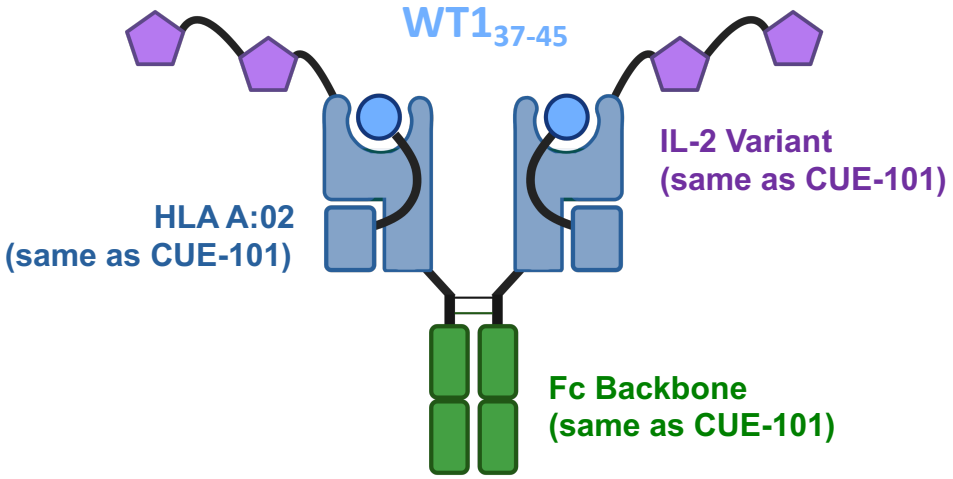
- First line HPV+ Head and Neck cancer in combination with pembrolizumab

Neoadjuvant therapy

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

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

Molecular Design



Clinical Rationale

- Top ranked cancer antigen by the National Cancer Institute (NCI)
- WT1 is a known tumor driver with low risk of immune escape as the tumor is dependent upon WT1's oncogenic role
- No reports indicative of autoimmune or off-target reactions in mice or humans after administration of WT1-targeted immunotherapy (prior human experience with peptide & DC vaccines, cell therapy)

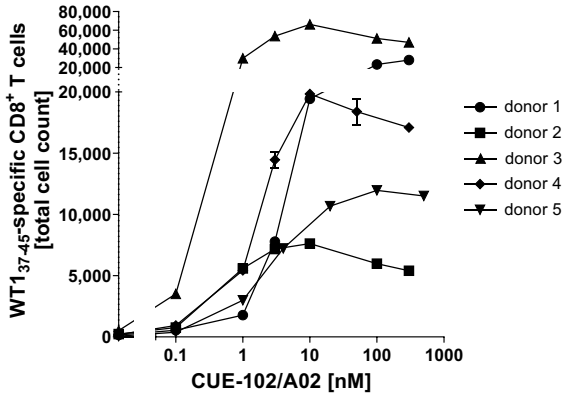
Clinical Opportunity

- WT1 is expressed in over 20 types of hematological malignancies and solid tumors offering broad commercialization opportunity

CUE-102: Supporting Biology and Nonclinical Data

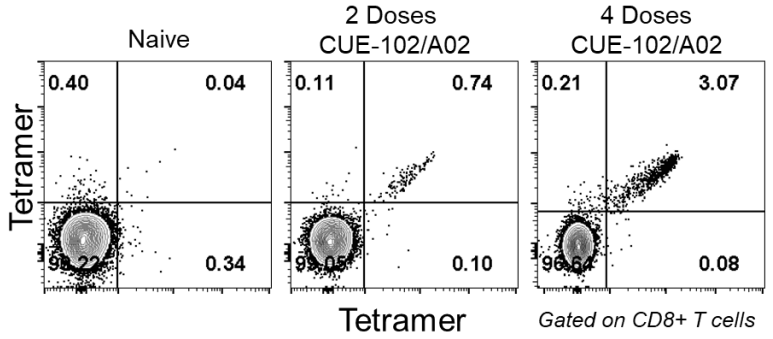
Priming and expansion of $WT1_{37-45}$-specific $CD8^+$ T cells in vitro and in vivo

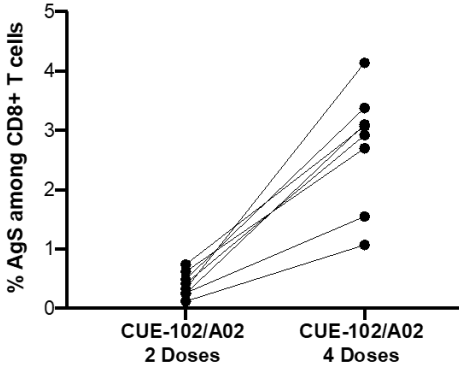
T cell expansion in vitro



Naïve HLA-A2 Transgenic Mice

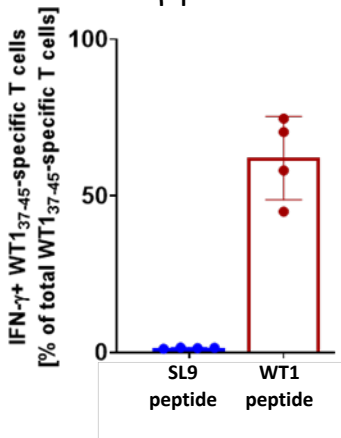
T cell priming and expansion in vivo



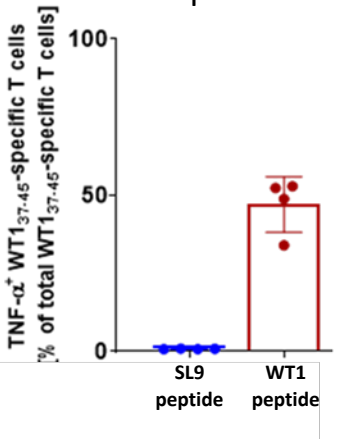


Polyfunctionality and CTL activity of the CUE-102-induced T cell repertoire in vitro and in vivo

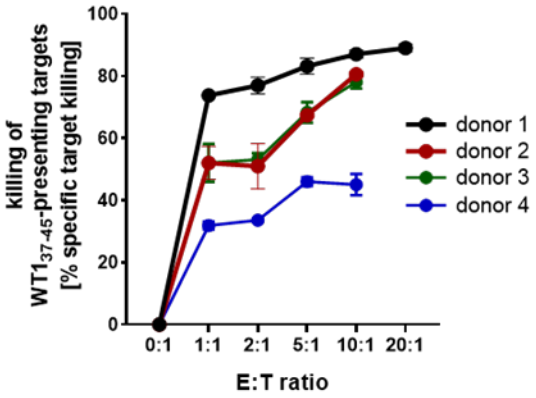
IFN-γ production



TNF-α production

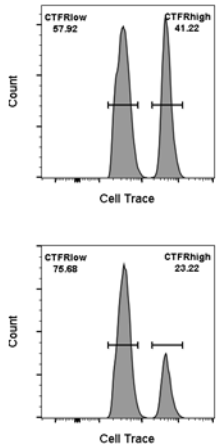


Target cell killing

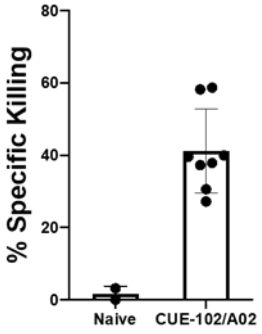


Naive

CUE-102/A02 immunized



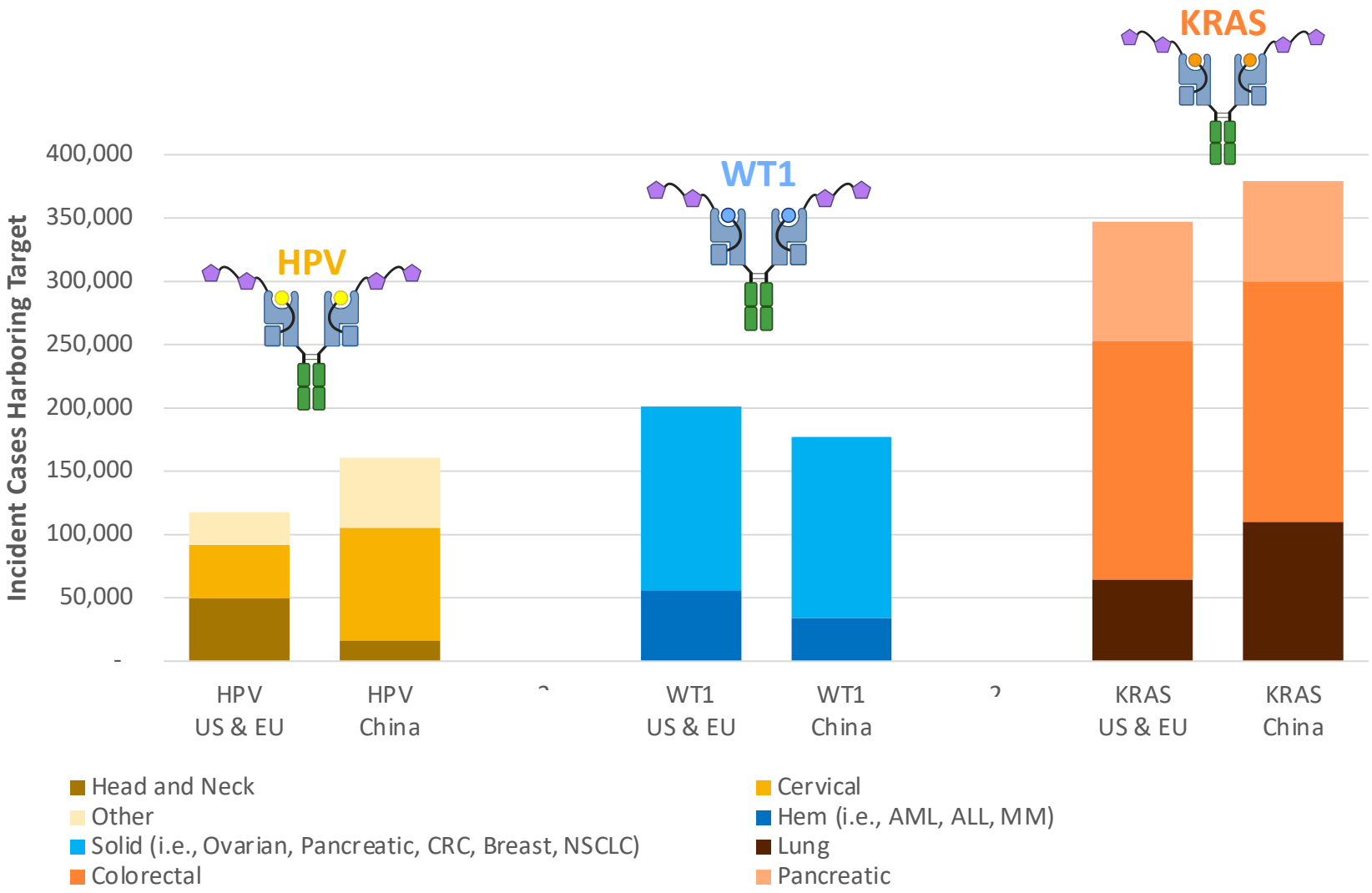
In vivo CTL activity



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

Broad Universe of Addressable TCR Targets with the CUE-100 Series

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



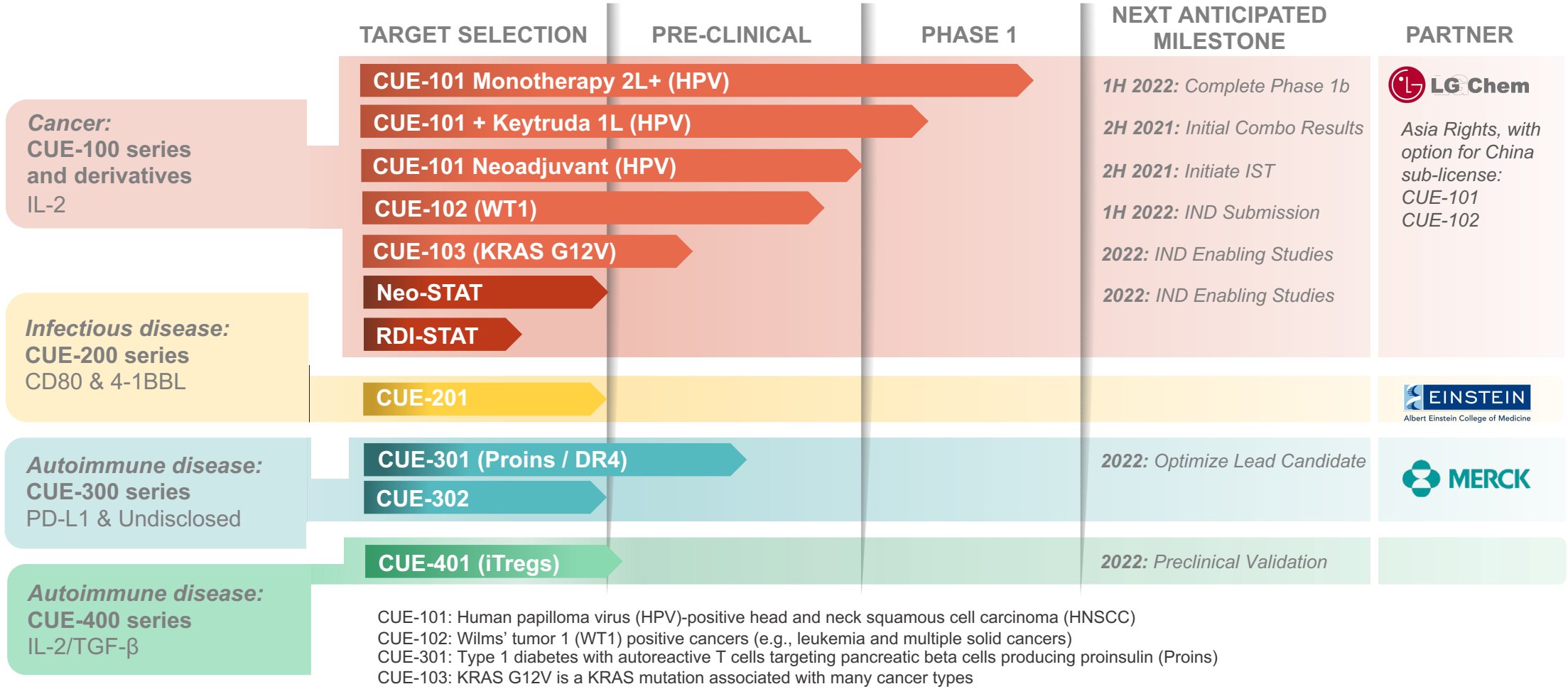
Sources (Accessed 2020)
Annual Incidence: SEER (US), Globocan (EU and China)
Antigen Expression: NIH TGCA, Cancer Atlas

Cue Biopharma, Inc: Q2 2021 Financial Highlights

Cue Biopharma, Inc. Selected Consolidated Statement of Operations Data (in thousands)				
	Three Months Ended June 30,			
	2021		2020	
Collaboration revenue	$	2,739	$	1,075
Operating expenses:				
General and administrative		4,280		3,898
Research and development		8,762		8,119
Total operating expenses		13,042		12,017
Loss from operations	$	(10,303)	$	(10,942)
Other income:				
Interest income, net		24		109
Net Loss	$	(10,279)	$	(10,833)
Net loss per common share – basic and diluted	$	(0.33)	$	(0.38)
Weighted average common shares outstanding – basic and diluted		31,233,794		28,221,537

Cue Biopharma, Inc. Selected Consolidated Balance Sheet Data (in thousands)				
	June 30, 2021		December 31, 2020	
Cash and cash equivalents	$	73,920	$	74,866
Marketable securities		-		10,003
Total current assets	$	79,677	$	87,527
Working Capital	$	63,004	$	71,212
Total assets	$	89,672	$	99,533
Total Stockholders' equity	$	72,910	$	78,911

Cue Biopharma Drug Product Candidate Pipeline

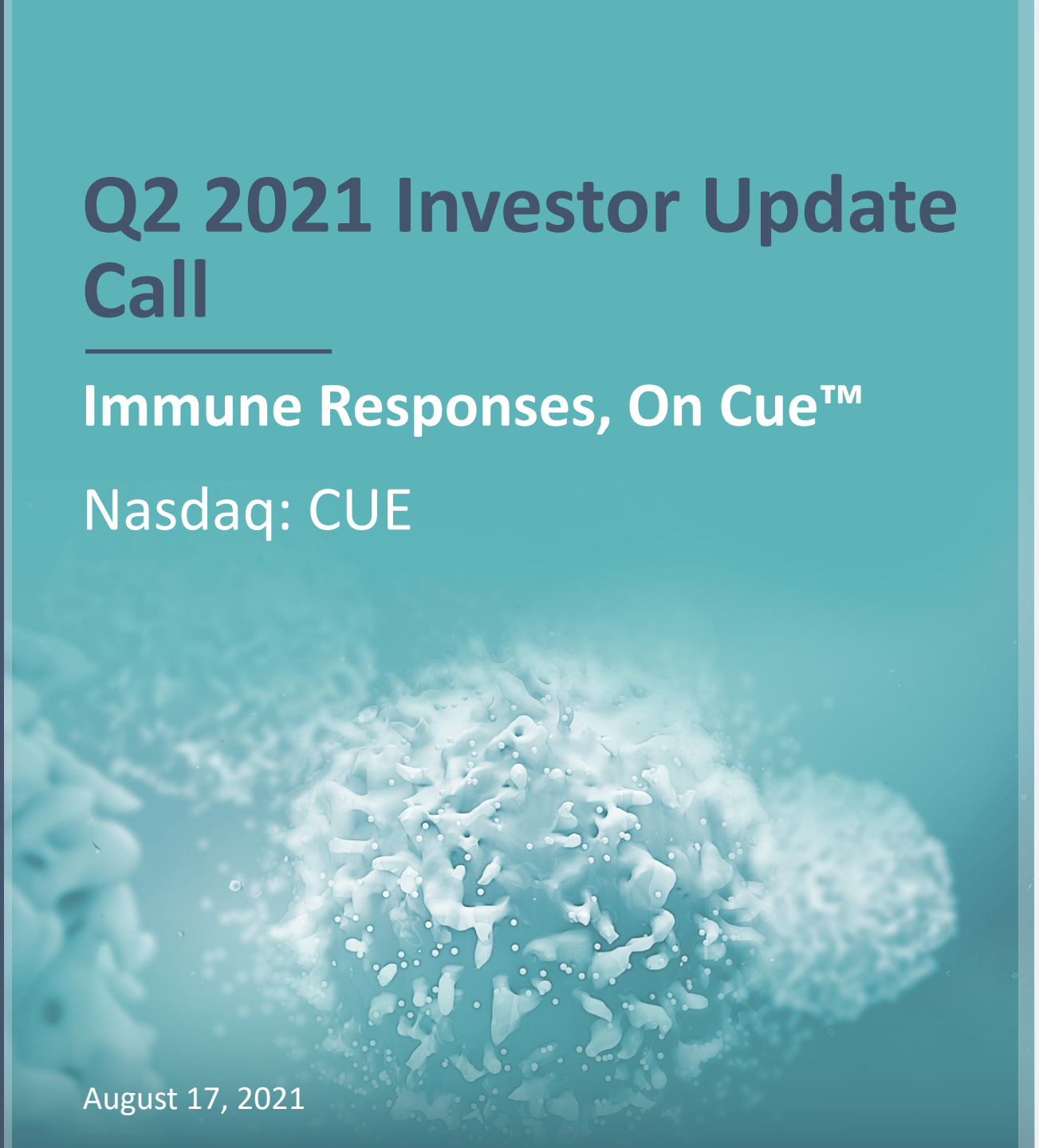


CUE-101: Human papilloma virus (HPV)-positive head and neck squamous cell carcinoma (HNSCC)
CUE-102: Wilms' tumor 1 (WT1) positive cancers (e.g., leukemia and multiple solid cancers)
CUE-301: Type 1 diabetes with autoreactive T cells targeting pancreatic beta cells producing proinsulin (Proins)
CUE-103: KRAS G12V is a KRAS mutation associated with many cancer types
CUE-401: Rheumatologic and gastrointestinal autoimmune/inflammatory disorders, GvHD
IST: Investigator-sponsored trial

Q2 2021 Investor Update Call

Immune Responses, On Cue™

Nasdaq: CUE



August 17, 2021

CUE™ BIOPHARMA