Q3 Investor/Earnings Call

Immune Responses, On Cue™

Harnessing the Potential of the Human Immune System to Treat Cancer

Nasdaq: CUE

November 14, 2022

CUE™ BIOPHARMA

Disclaimers

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Agenda

• **Introduction**	Dan Passeri, CEO
• **Immuno-STATS:** TCR-selective Engagers	Anish Suri, President and CSO
• **Clinical Update**	Dr. Ken Pienta, Acting CMO
– CUE-101: Representative of IL-2 based CUE-100 series	Dr. Matteo Levisetti, SVP, Clin. Development
– CUE-102: Targeting WT1+ cancers	
• **3Q-FY22 Financial Results**	Kerri-Ann Millar, CFO
• **Concluding Remarks**	Dan Passeri, CEO
• **Q&A**	All

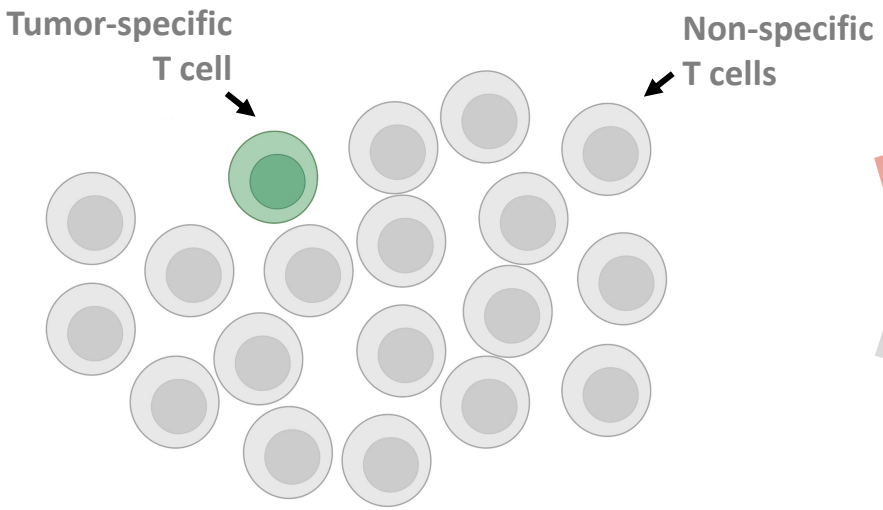
Immuno-STAT™ (IST) Platform: TCR-selective Engagers of Tumor-specific T cells

- **CUE-100 Series: TCR engagers that selectively target IL-2 to tumor-specific T cells**
  - *Creates a therapeutic index for harnessing the potential of IL-2 in immuno-oncology*
- **Clinical Validation via CUE-101 (HPV+ R/M HNSCC)**
  - *Monotherapy efficacy in late-stage 3L+ patients (RECIST-based OR and SDs; significant increase in mOS)*
  - *Combination Tx with CPI in 1L patients (current RECIST-based 40% ORR at RP2D, and SDs; survival data maturing)*
  - *Favorable tolerability profile observed to date (>65 patients dosed across mono-tx and combo-tx trials)*
- **Platform modularity enables efficient pipeline expansion into multiple cancers**
  - *CUE-102 (WT-1: CRC, Gastric, Pancreatic, Ovarian) de-risked by CUE-101 clinical data: Ph 1 ongoing*
  - *Phase 1 dose escalation shortened due in part to favorable tolerability profile demonstrated to date by CUE-101*
  - *Neo-STAT™ enables targeting multiple tumor Ags to maximize time and cost efficiencies to expand pipeline*
- **Milestones and potential value drivers**
  - *CUE-101 Monotherapy mOS potential registration path*
  - *CUE-101 Combination with Pembrolizumab to date ORR ≥ 40% / mOS supports potential registration path*

CUE BIOPHARMA

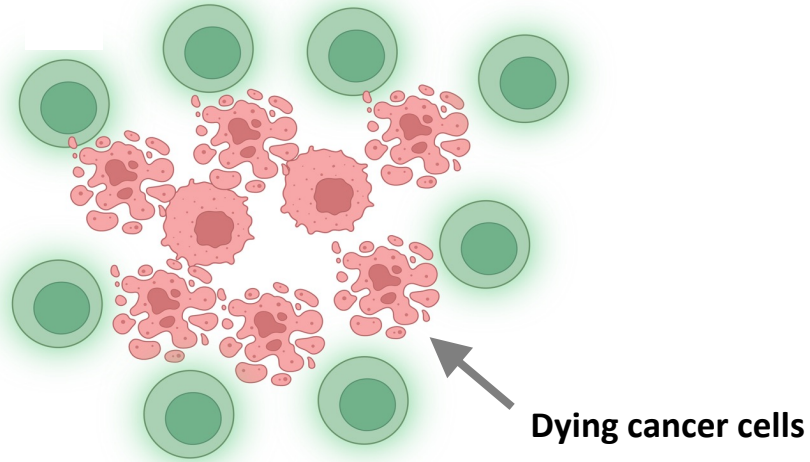
Tumor-specific T cells are *Key* for Successful Immunotherapy of Cancers

A minute fraction of the patient's baseline T cell repertoire (~ <0.1%) is tumor-specific



Immuno-STAT Platform
Selective activation of tumor-specific T cells

Non-selective Modulation
E.g., CPIs, cytokines, bispecifics



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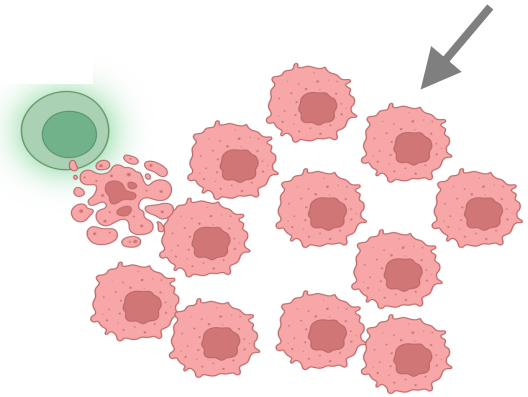
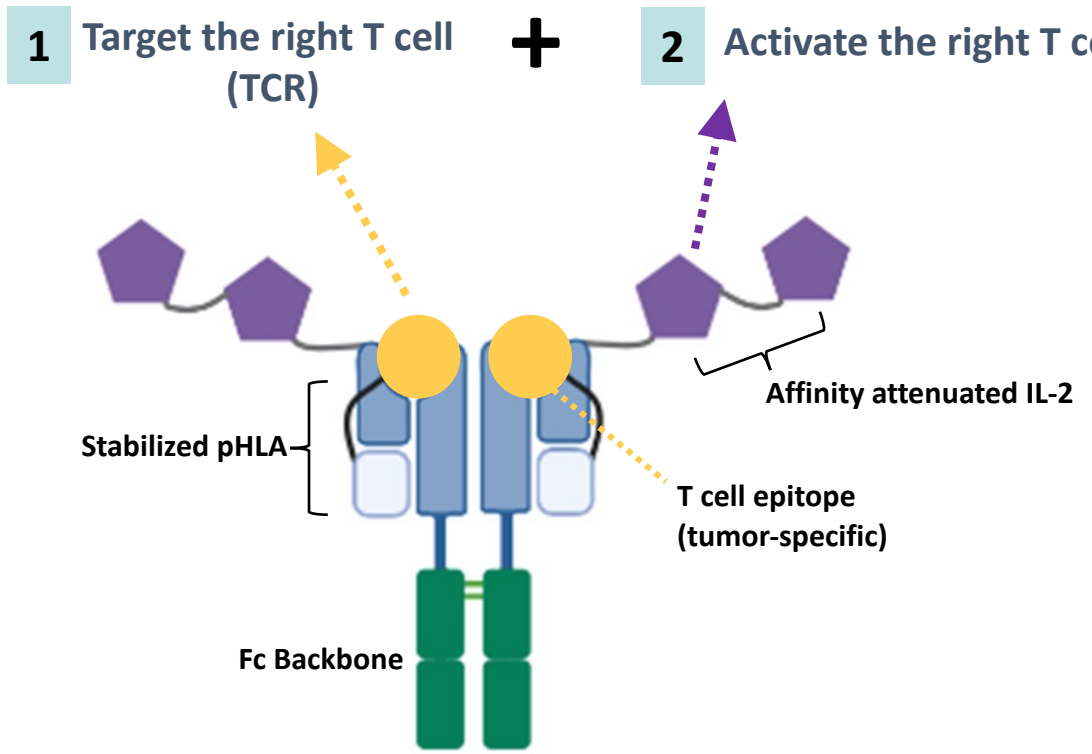


- The T cell receptor (TCR) is the ***only unique marker*** of a tumor-specific T cell
- The ***Immuno-STAT platform*** is designed to harness the **TCR specificity** to selectively activate anti-tumor T cells

CUE-100 Series ISTs: TCR-selective targeting of IL-2 to Tumor-specific T cells

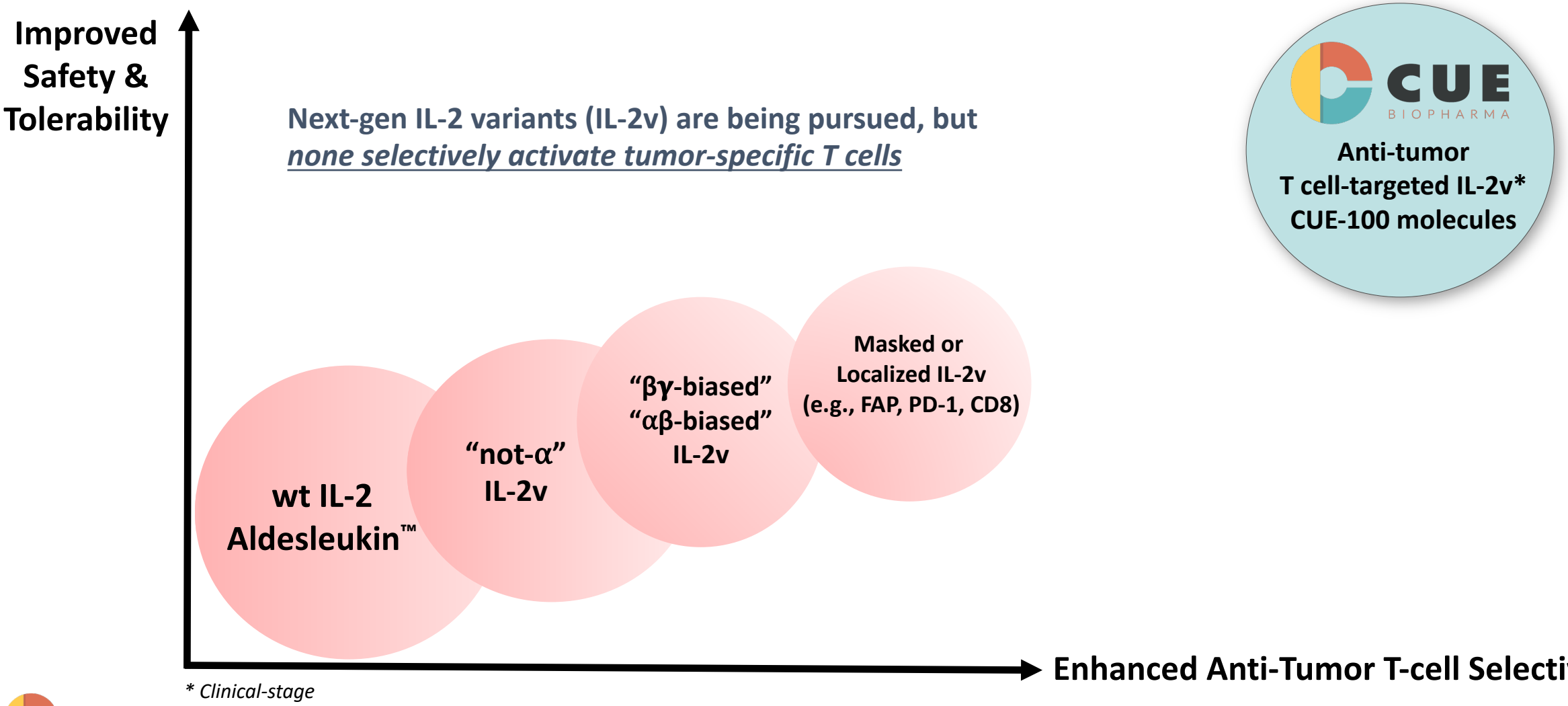


CUE-100 Series Design

- **Single biologic molecule**
- **Ab-like manufacturability and CMC**
- **Stable, off-the-shelf**
- **IV (or SC) administration**

- ✓ Designed to Harness *TCR-specificity* of anti-tumor T cells
- ✓ Engagement of the "right T cell" results in co-stimulation of TCR and IL-2 receptor (IL-2R)
- ✓ Limits systemic activation of irrelevant T cells
- ✓ *Designed to create a therapeutic index for IL-2*
- ✓ Provides PoC and mechanistic basis for targeting numerous other cytokines and activation signals

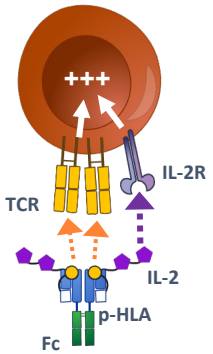
CUE-100 Series: Potential for Best-in-Class IL-2

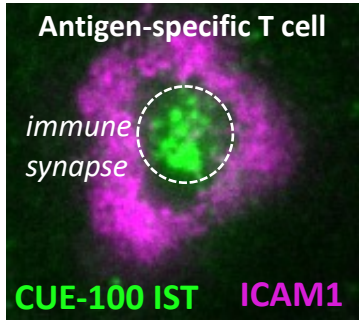


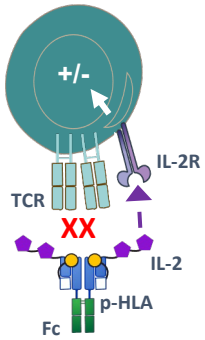
** Clinical-stage*

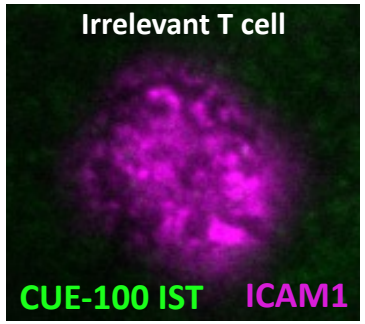
CUE-100 Series ISTs: Selectivity and Activity

Selective Engagement (Immune Synapse)



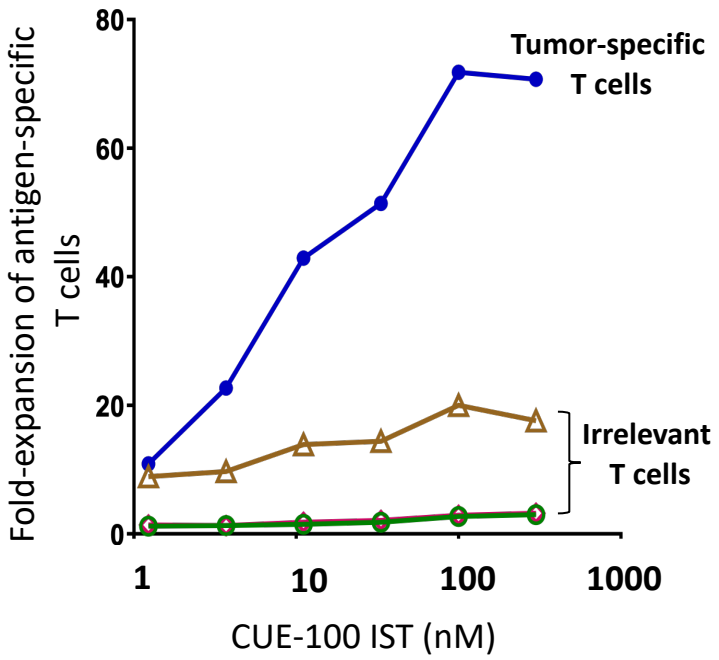




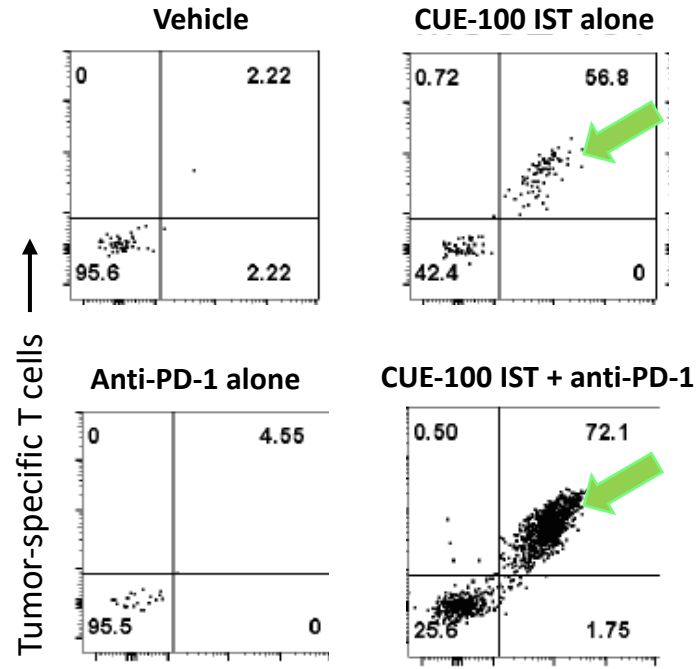


Collaboration with Dr. Michael Dustin, Univ. of Oxford

Selective Expansion (Tumor-specific T cells)

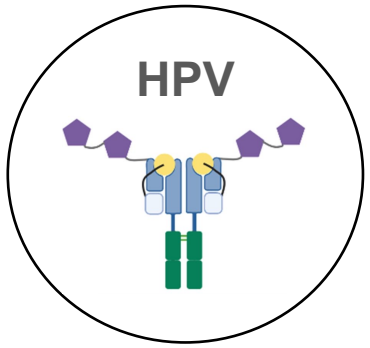


T cell Activation in Tumors ("hot tumors")



Quayle et al Clin Can Res 2020

CUE-101 Provides Clinical PoC and Platform De-risking



CUE-101

Head & Neck*
Anal
Cervical
Penile
Vulvar

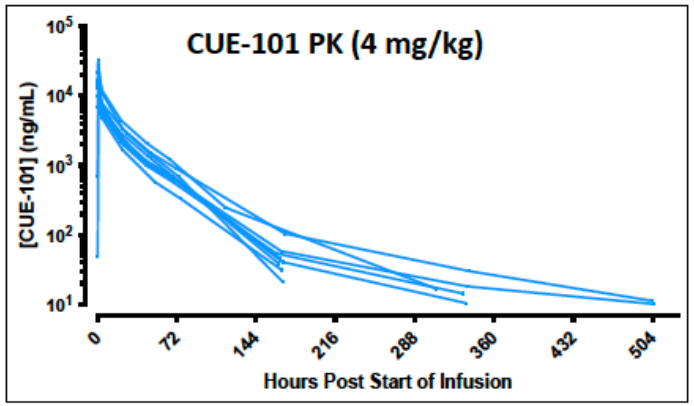
** Ongoing clinical trial*

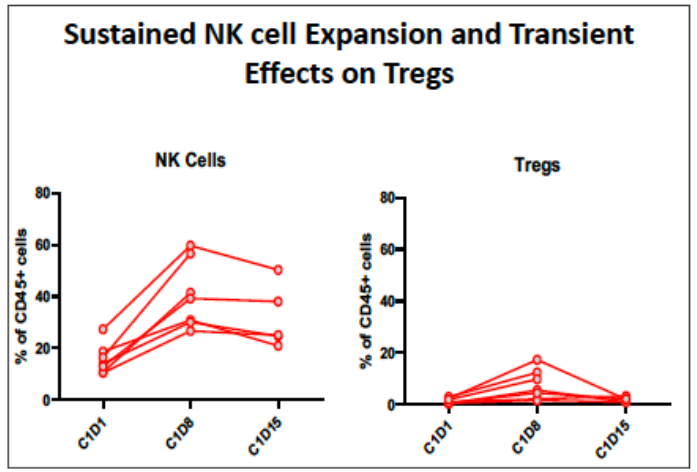
- CUE-101 Monotherapy in 3L+ R/M HNSCC
- CUE-101 + Pembrolizumab Combination in 1L R/M HNSCC
- CUE-101 Neo-adjuvant trial in locally/advanced HNSCC
  - Trial ongoing at Washington University in St. Louis

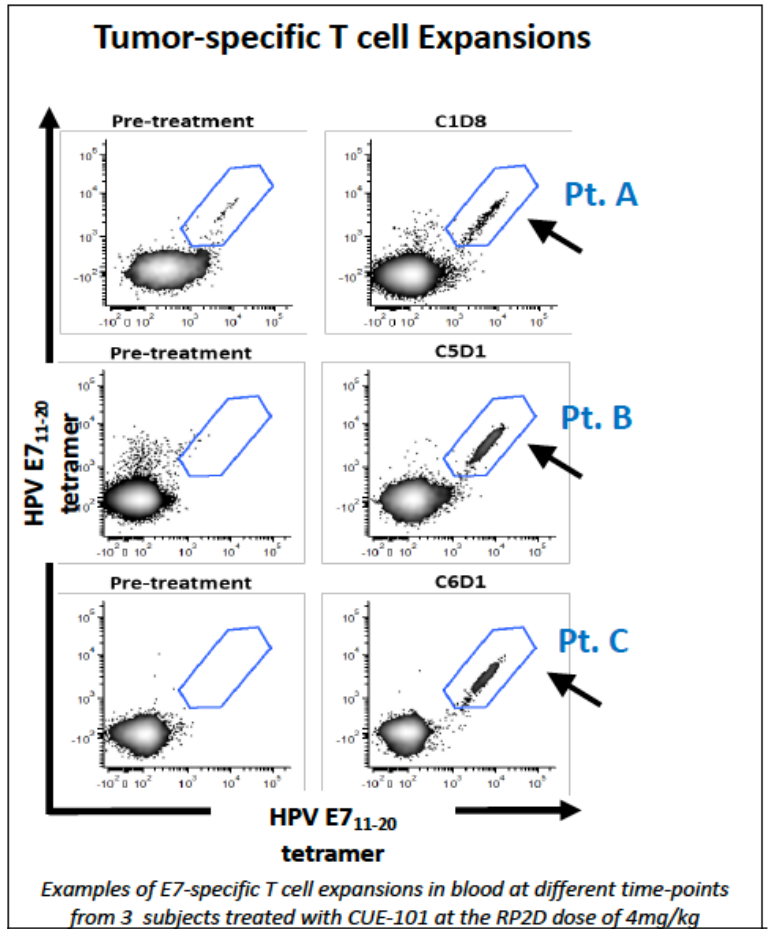
CUE-101: Monotherapy Efficacy in 3L+ R/M HNSCC Patients

- ✓ Demonstration of single-agent anti-tumor efficacy
  - *RECIST-based PR and Durable Stable Disease in 3L+ R/M HNSCC patients*
  - mOS benefit emerging from survival follow-up
- ✓ Selective expansion of tumor-specific T cells and NK cells
- ✓ T cell infiltration into tumor and increased tumor necrosis
- ✓ Tolerability at clinically active doses
- ✓ Sustained drug exposure upon repeated dosing with no clinical evidence of immunogenicity to date
- ✓ Fast Track Designation granted

CUE-101 Monotherapy Patient Data: PK, PD and Tumor Infiltration

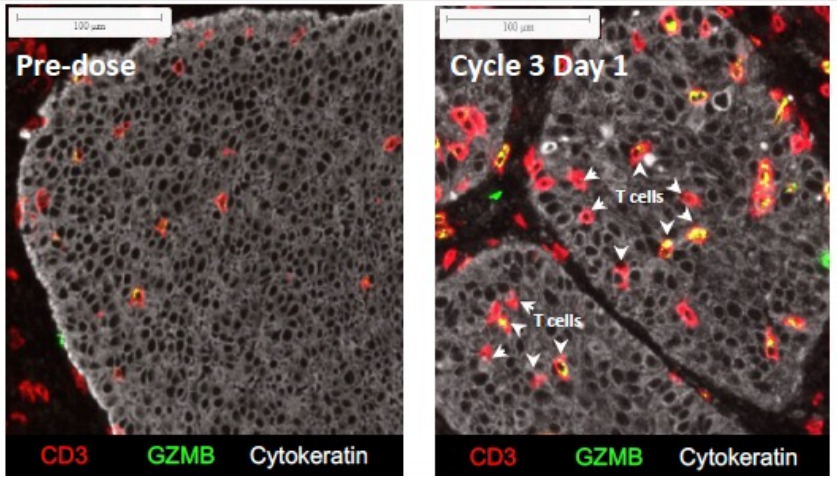




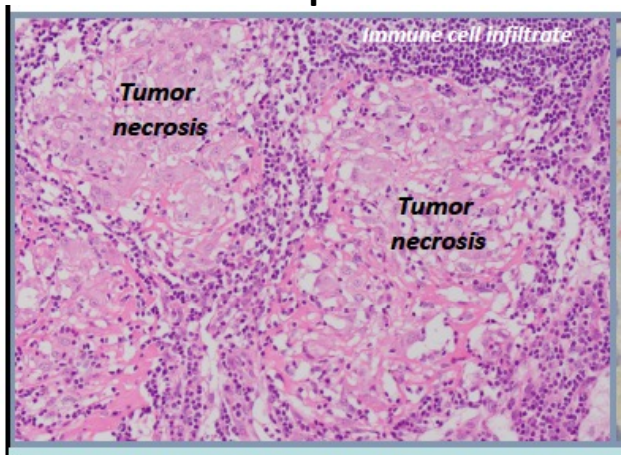


Examples of E7-specific T cell expansions in blood at different time-points from 3 subjects treated with CUE-101 at the RP2D dose of 4mg/kg

T cell infiltration into tumors post-CUE-101 Tx

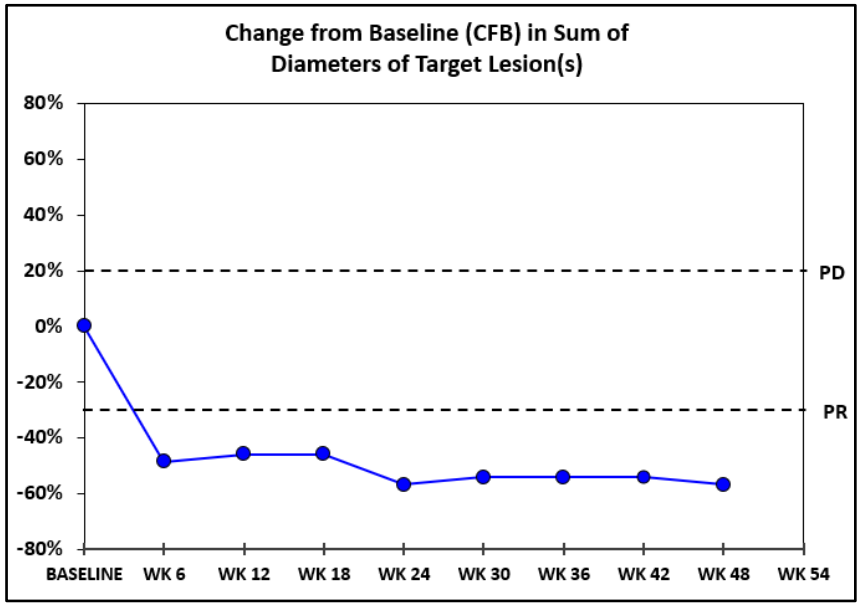


Tumor necrosis post-CUE-101 Tx



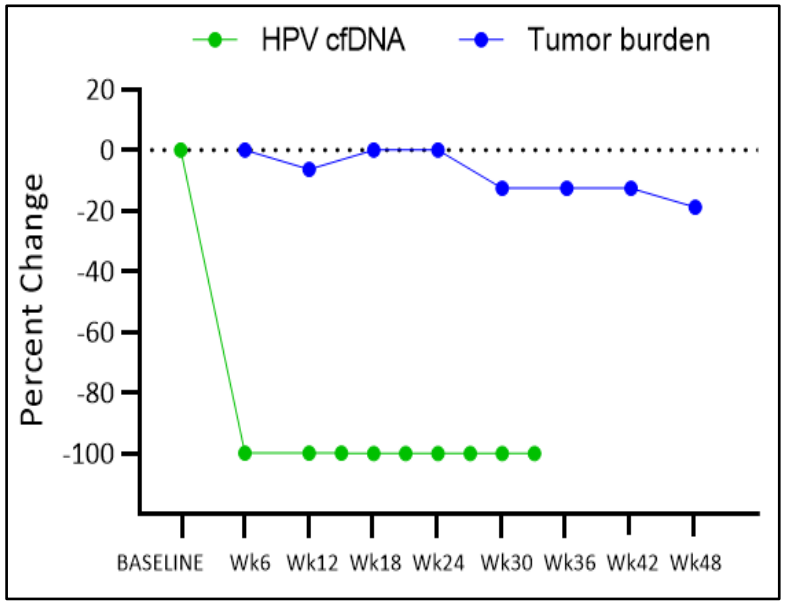
Patterns of Clinical Efficacy in Patients with CUE-101 Monotherapy

Patient A



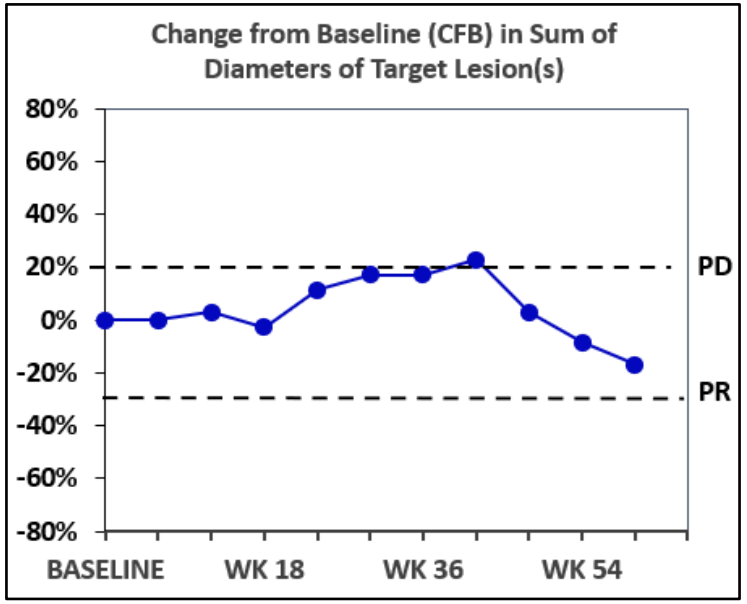
- Rapid tumor reduction and durable PR
- On treatment ~ 1 year

Patient B



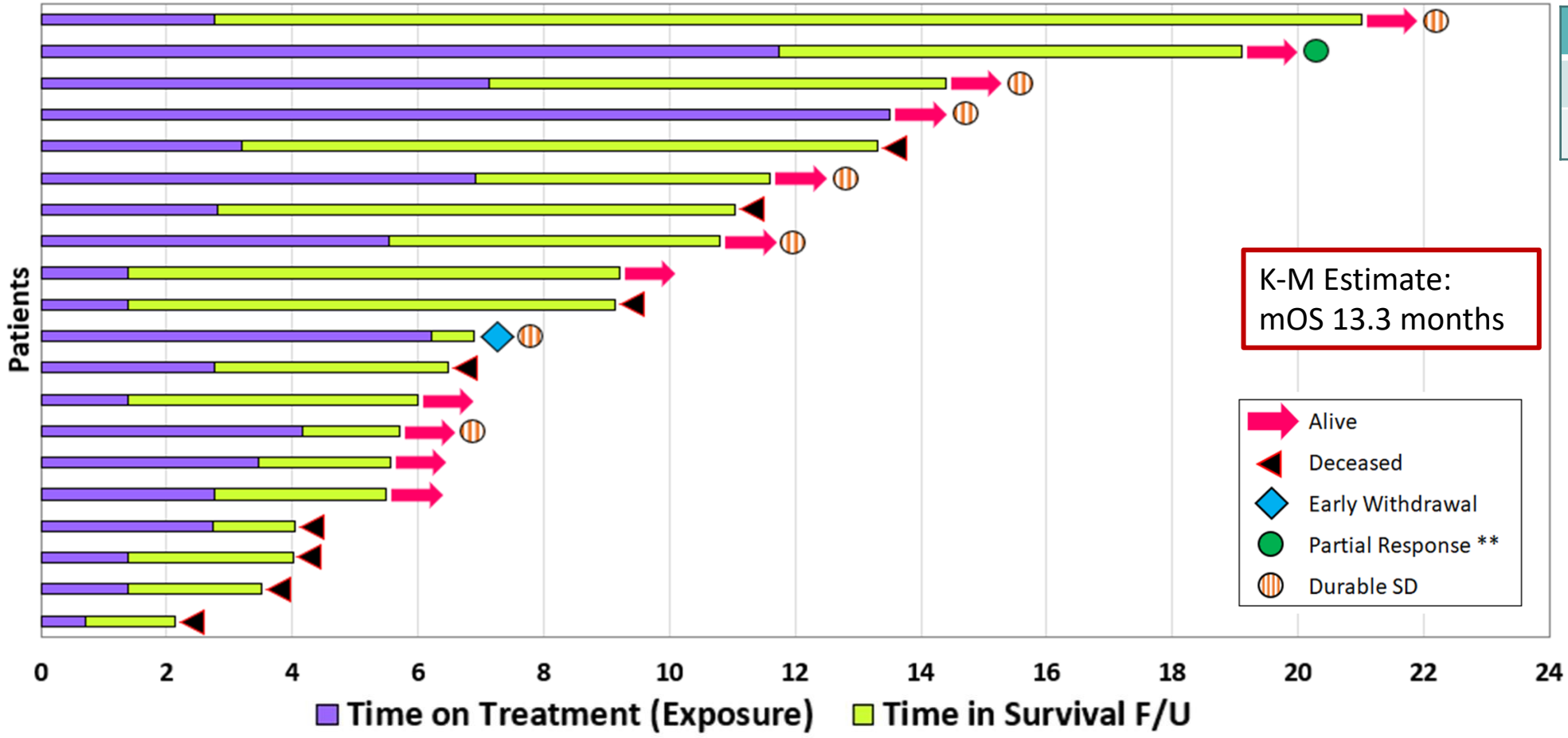
- Durable SD which may be pathologic CR
- Remains on treatment > 1 year with no evidence of HPV cfDNA

Patient C



- Durable SD
- Remains on treatment > 1 year

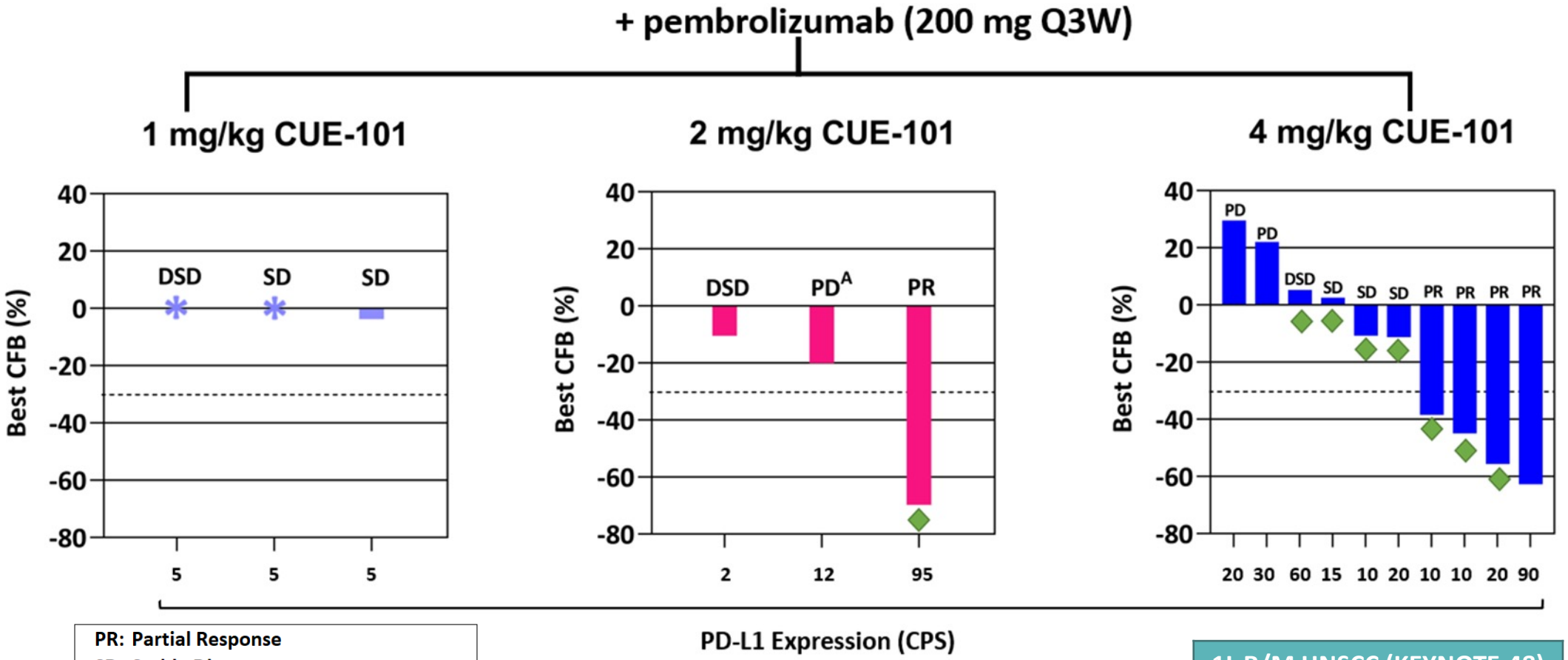
Increased Overall Survival in 3L+ Patients Treated with CUE-101 Monotherapy (n=20)



2L R/M HNSCC (KEYNOTE-40)	
mOS	8.4 months
Lancet 2018	

Overall survival in months for all monotherapy patients treated in CUE-101-01, at 4 mg/kg, from time of 1st dose of drug (Cycle 1 Day 1). PR (partial response) is indicated by a green circle; Durable SD (stable disease) is indicated by a hatched orange circle (requires SD at ≥ 2 consecutive scans at 6-week and 12-week visits). ** Onset and duration of the response is not indicated on the plot. Kaplan-Meier Analysis CUE-101 mOS 13.3 month; [95% Confidence Interval (9.1, NA)].

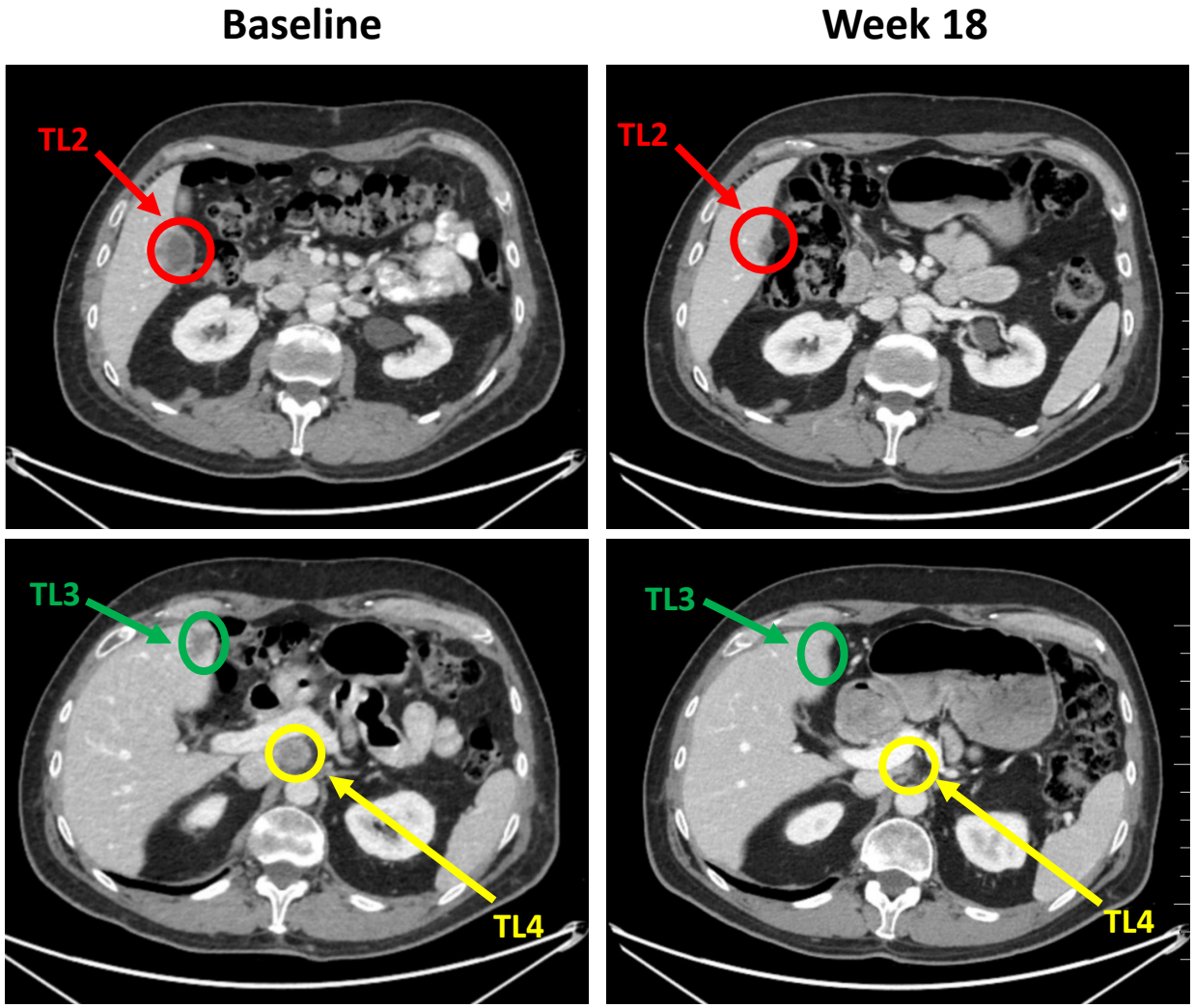
CUE-101 in Combination with Pembrolizumab in 1L R/M HNSCC: 40% ORR at 4 mg/kg RP2D

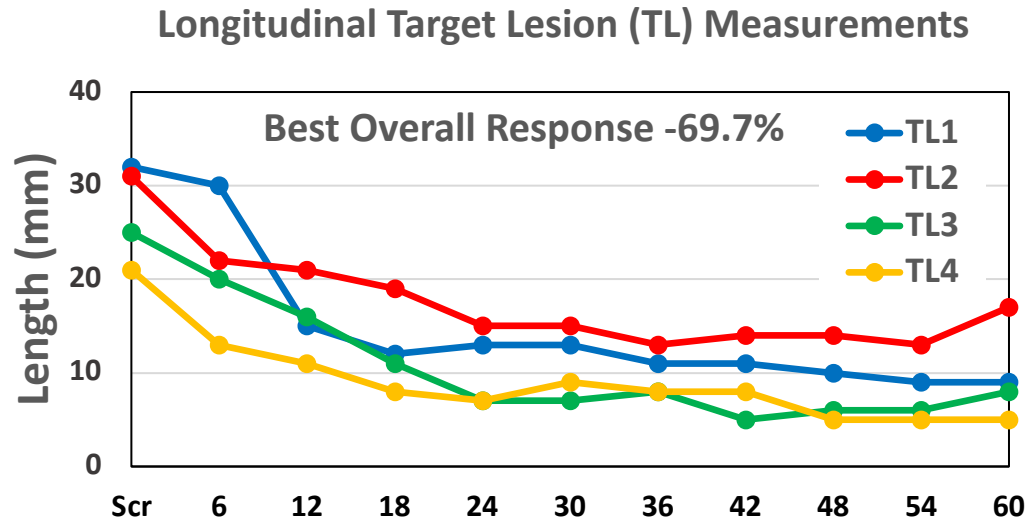


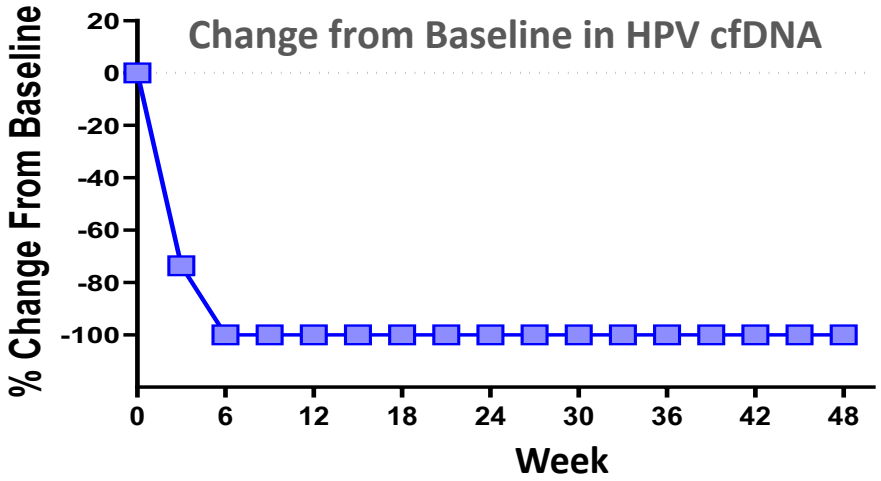
PR: Partial Response
SD: Stable Disease
DSD: Durable Stable Disease
PD: Progressive Disease
A: PD at C3 in non-targets, targets stable
✱ : Best CFB = 0%
◆ : Ongoing on treatment

1L R/M HNSCC (KEYNOTE-48)	
Pembro ORR	19%
Lancet 2019	

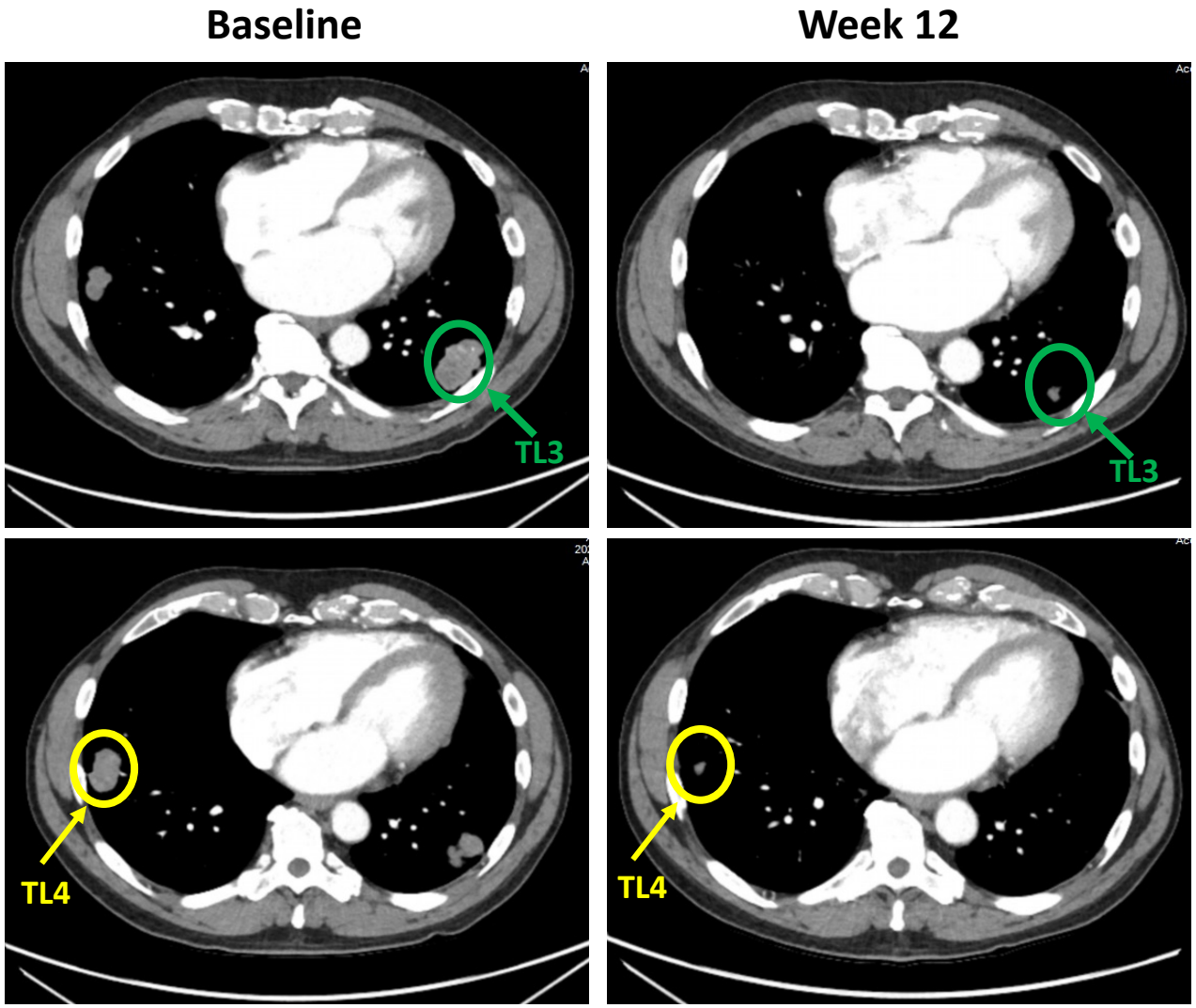
CUE-101: Case Study – Confirmed PR in Combo Patient (2 mg/kg + pembrolizumab)

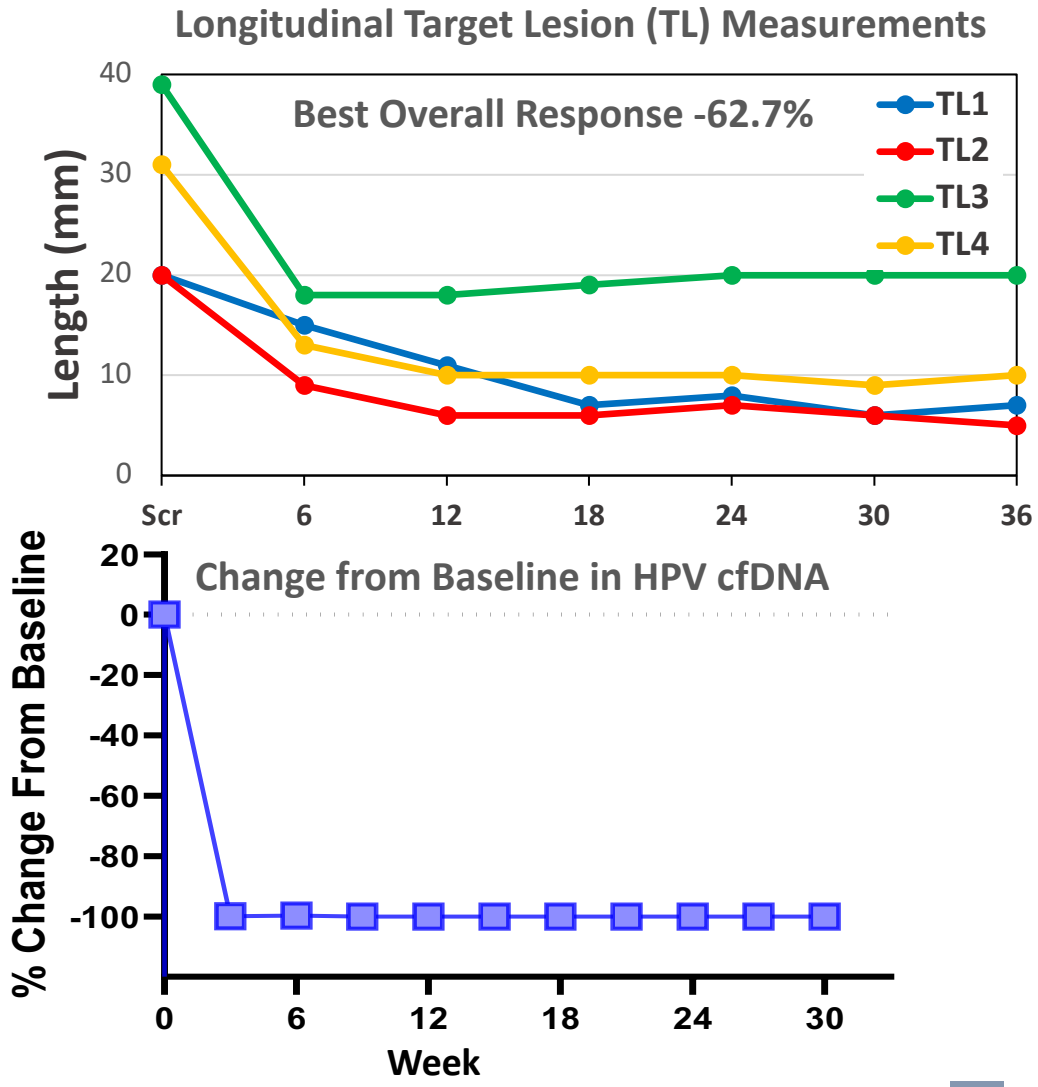




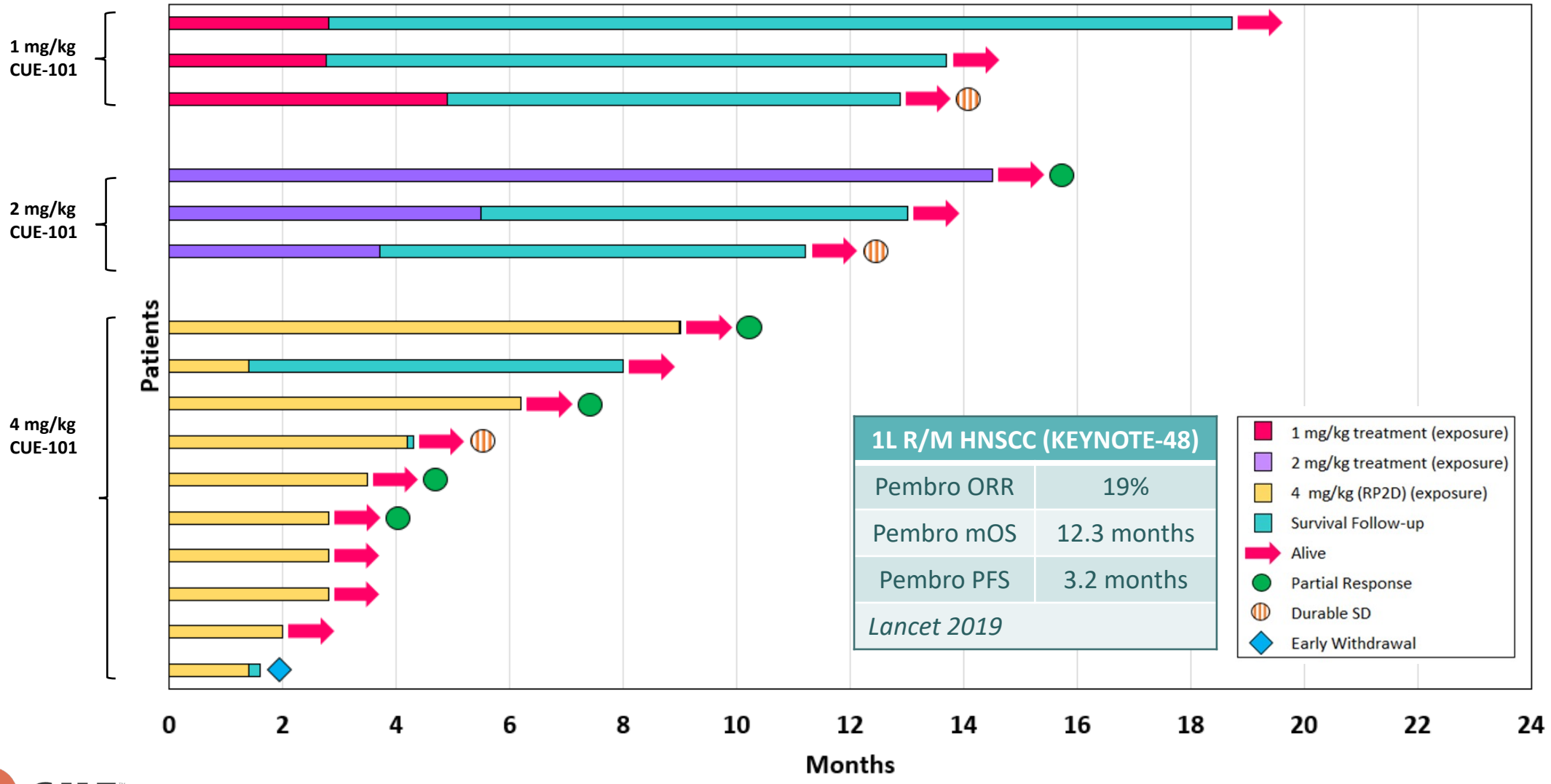


CUE-101: Case Study – Confirmed PR in Combo Patient (4 mg/kg + pembrolizumab)





Overall Survival by Dose in CUE-101 Combination Therapy Patients



Registrational Path Options

- **CUE-101 Monotherapy**
  - Fast Track Designation granted for the treatment of R/M HPV+ HNSCC
  - Potential Phase 3 registrational trial option: CUE-101 vs. Investigator's Choice of chemotherapy in patients that have failed prior chemo and CPI, Primary Endpoint: Overall Survival
- **CUE-101 Combination therapy with pembrolizumab**
  - Fast Track Designation granted for the treatment of R/M HPV+ HNSCC
  - On track for completion of enrollment of expansion cohort (n=20)
  - Potential Phase 3 registrational trial option: CUE-101 + pembrolizumab vs pembrolizumab in 1L R/M HNSCC patients, Primary Endpoints: ORR, PFS; Secondary Endpoints: OS, PROs

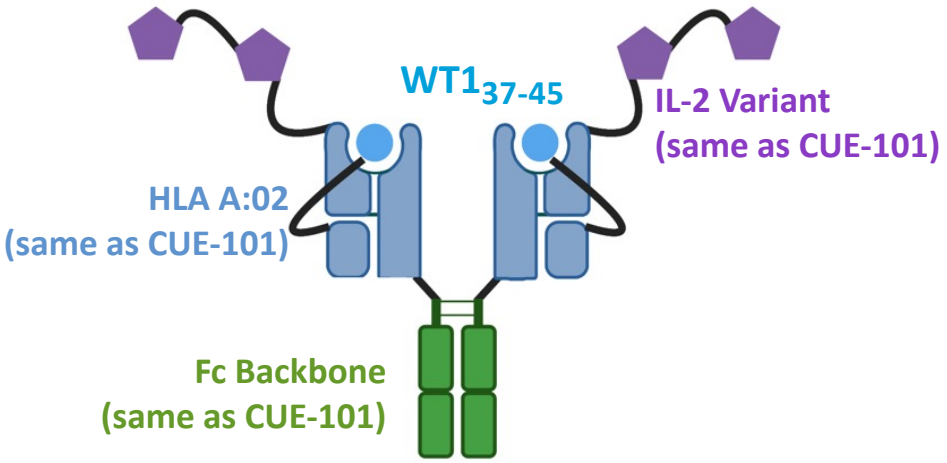
FDA Fast Track Designation (granted 10/03/2022) facilitates the development and expedited review of new drugs that treat a serious medical condition and fill an unmet medical need by providing:

- More frequent meetings and written communication with the FDA
- Eligibility for Accelerated Approval and Priority Review if criteria are met
- Rolling review

CUE BIOPHARMA

CUE-102 Wilms Tumor 1 (WT1): Broad Potential Opportunity in Multiple Solid and Heme Cancers

Molecular Design
(99% sequence identity to CUE-101)

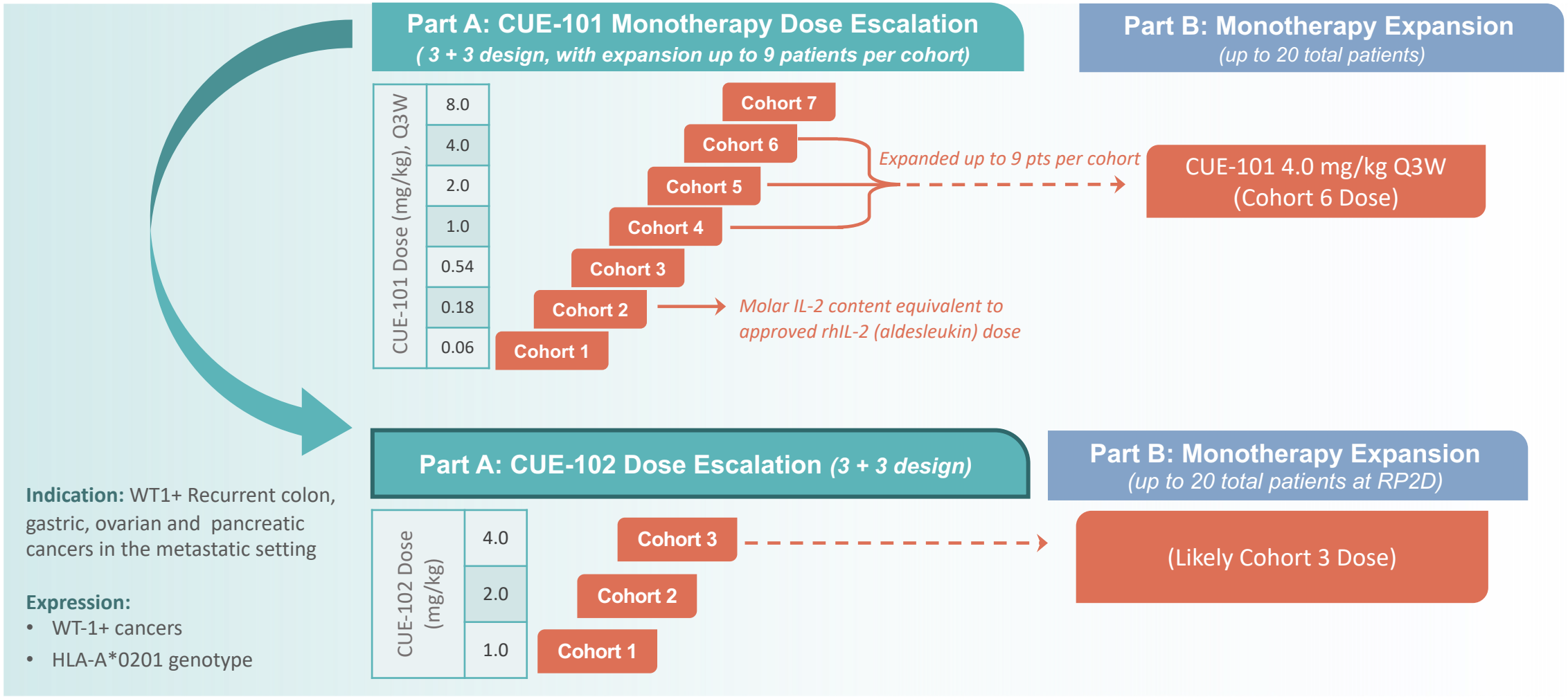


CUE-102

- IND approval for CUE-102 harnessed the clinical de-risking observed with CUE-101, leading to potential advantages:
  - *Clinical development efficiencies (approval to start at a higher dose and minimize cohorts for dose escalation)*
  - *Regulatory advantages (FDA did not require additional IND tox)*
- CUE-102 targets a dominant T cell epitope from WT1
- WT1 is an attractive onco-fetal tumor antigen with significant expression in numerous solid and heme cancers
  - *Solid: CRC, Ovarian, Lung, Gastric, Pancreatic, Breast, GBM*
  - *Heme: AML/MDS, ALL, MM*

Phase 1 Monotherapy Trial Currently Enrolling (NCT05360680)

CUE-101 Accelerates CUE-102 Clinical Development by Enabling Dose Escalation to Start at 1 mg/ kg



Indication: WT1+ Recurrent colon, gastric, ovarian and pancreatic cancers in the metastatic setting

Expression:

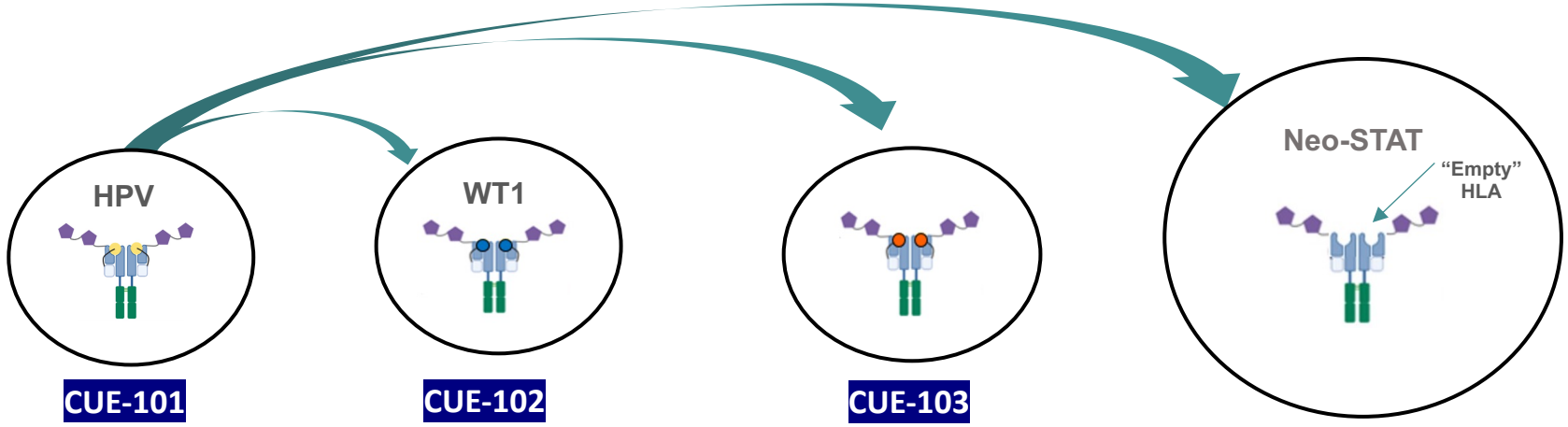
- WT-1+ cancers
- HLA-A*0201 genotype

Abbreviations: Q3W, once every 3 weeks; rhIL-2, recombinant human interleukin-2; RP2D, Recommended Phase 2 Dose

CUE-100 Series: Broad Potential Opportunities in Cancer Immunotherapy

We believe clinical PoC with CUE-101 de-risks and validates CUE-100 series

Structural similarity creates potential regulatory and development efficiencies



CUE-101	CUE-102		CUE-103		
Head & Neck*	**Solid**	**Heme**	**HLA A02**:	**HLA A11/A03**:	**Multiple Tumor Epitopes**
Anal	**CRC***	AML	MAGE-A4	KRAS G12V	**Multiple HLA Alleles**
Cervical	**Gastric***	MDS	NY-ESO	KRAS G12D	
Penile	**Ovarian***	ALL	PRAME		
Vulvar	**Pancreatic***	MM	Etc.		
	Lung				
	Breast				
	GBM				

** Ongoing clinical trials*

Initial focus on validated, dominant tumor antigens

Cue Biopharma, Inc: Q3 2022 Financial Highlights

Cue Biopharma, Inc.
Selected Consolidated Statement of Operations Data
(in thousands, except share data)

	Three Months Ended September 30,	
	2022	2021
Collaboration revenue	$ 68	$ 2,395
Operating expenses:		
General and administrative	3,528	4,125
Research and development	7,571	11,288
Total operating expenses	11,099	15,413
Loss from operations	(11,031)	(13,018)
Other income:		
Total other income, net	76	25
Net Loss	$ (10,955)	$ (12,993)
Net loss per common share – basic and diluted	$ (0.31)	$ (0.41)
Weighted average common shares outstanding – basic and diluted	35,383,430	31,315,178

Cue Biopharma, Inc.
Selected Consolidated Balance Sheet Data
(in thousands)

	September 30, 2022	December 31, 2021
Cash and cash equivalents	29,726	64,371
Marketable securities	29,457	-
Total current assets	61,700	68,469
Working Capital	51,478	55,681
Total assets	76,300	83,401
Total Stockholders' equity	50,764	65,492

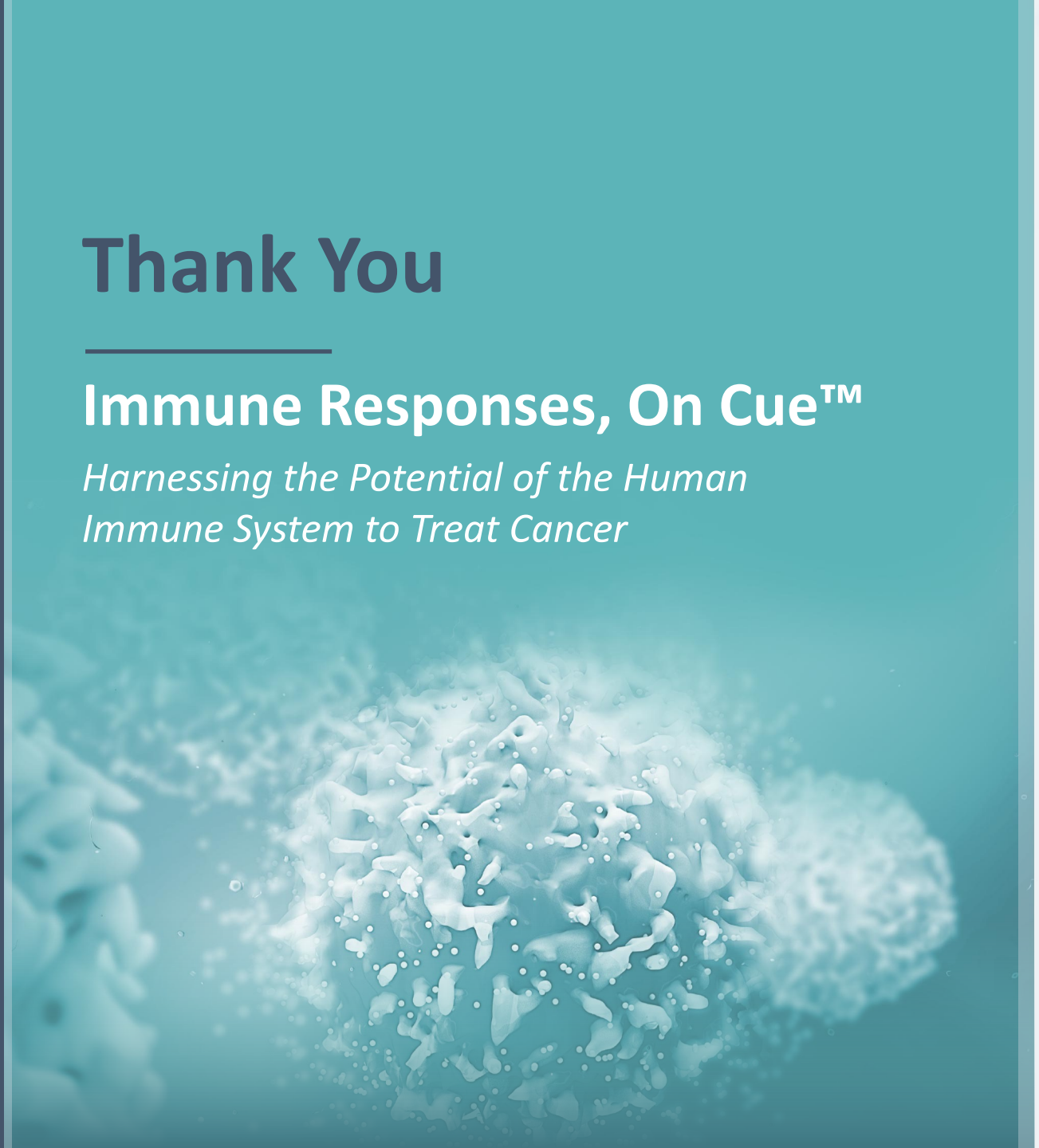
Upcoming Anticipated Key Milestones

- CUE-101 Monotherapy (mature mOS data EOY 2022 – define potential registrational trial mid 2023)
- CUE-101 + pembrolizumab Combination Therapy (preliminary ORR 2Q 2023 on 20 patients with potential registrational trial being defined by EOY 2023)
- CUE-102 Monotherapy (data from dose escalation by mid 2023-significant potential market opportunities for WT1 positive cancer indications)
- We believe maturing clinical datasets may catalyze significant BD/Corp Dev opportunities for pipeline expansion

Thank You

Immune Responses, On Cue™

Harnessing the Potential of the Human Immune System to Treat Cancer



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