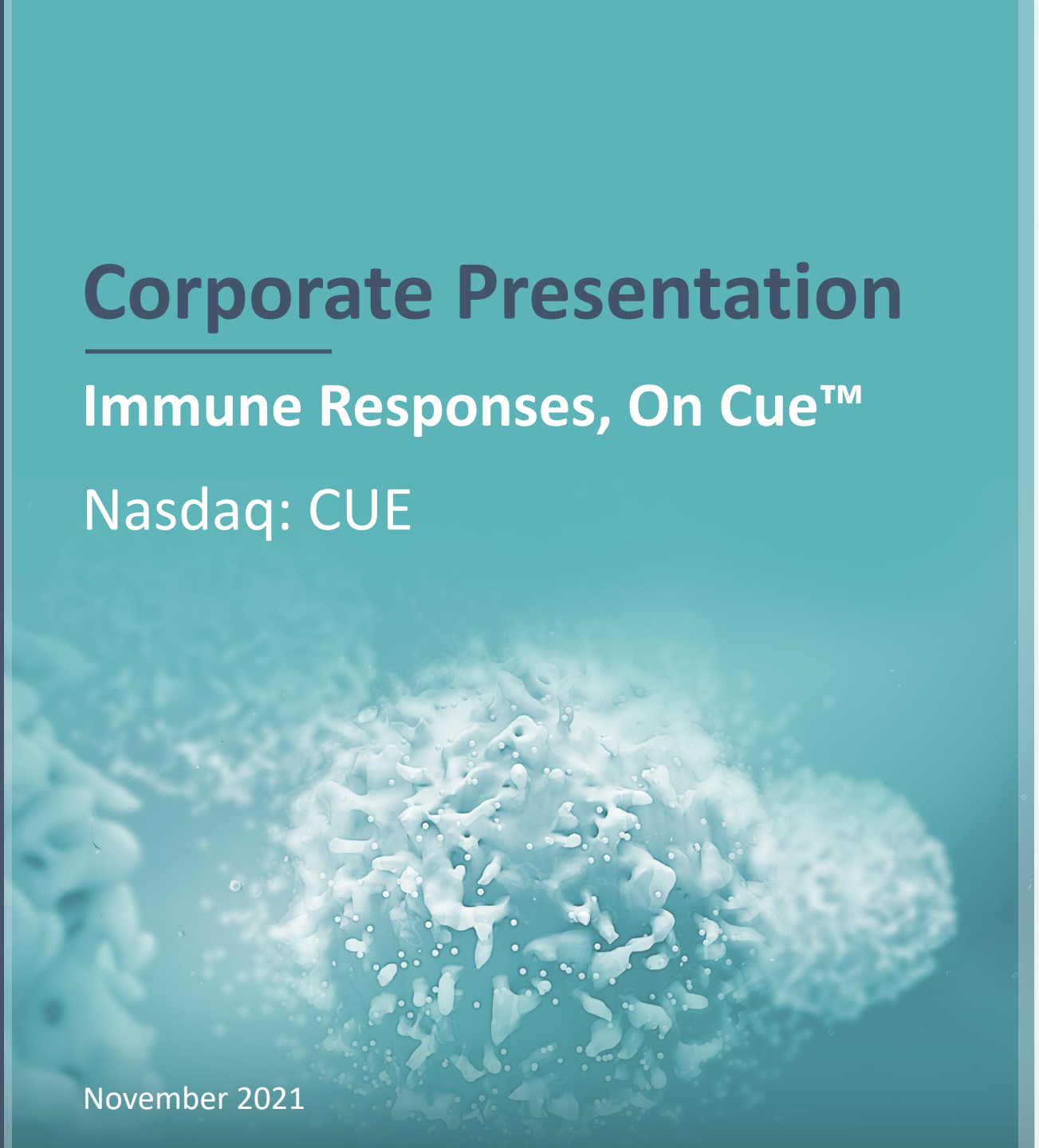
Corporate Presentation

Immune Responses, On Cue™

Nasdaq: CUE



November 2021

CUE™
BIOPHARMA

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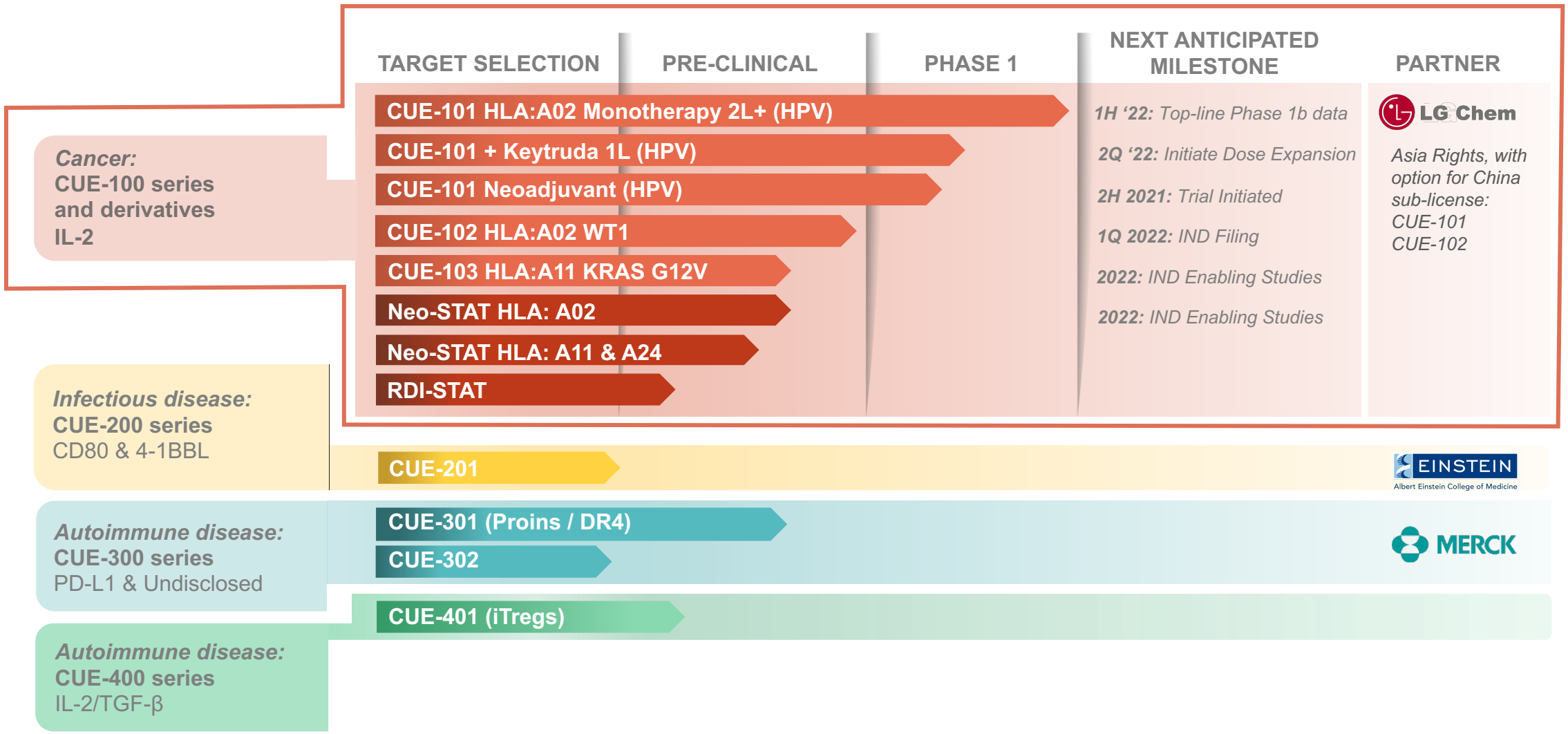
Cue Biopharma's Vision

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

CUE-100 Series: Changing the Therapeutic Landscape



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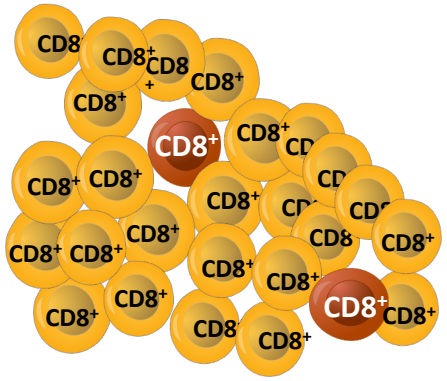
IL-2 Therapy Challenges: Non-selective Immune Activation = Poor Tolerability and Poor Therapeutic Performance

Wild Type IL-2 or IL-2 Variants

Example

- **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



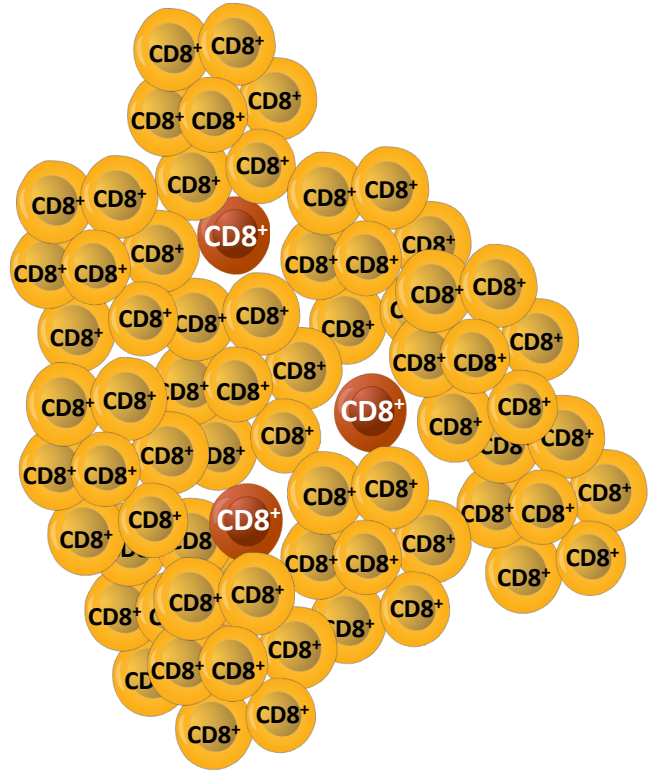
Considerations and Challenges

- **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.)

TUMOR-SPECIFIC CD8+ T CELL

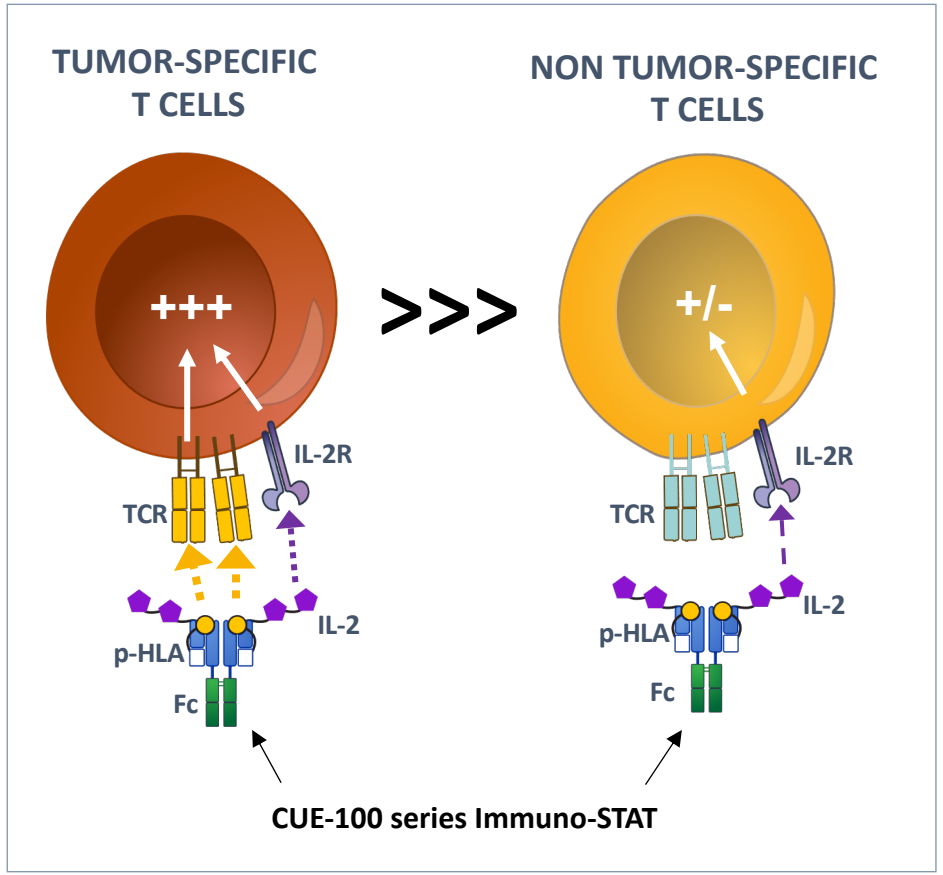
NON TUMOR-SPECIFIC CD8+ T CELL

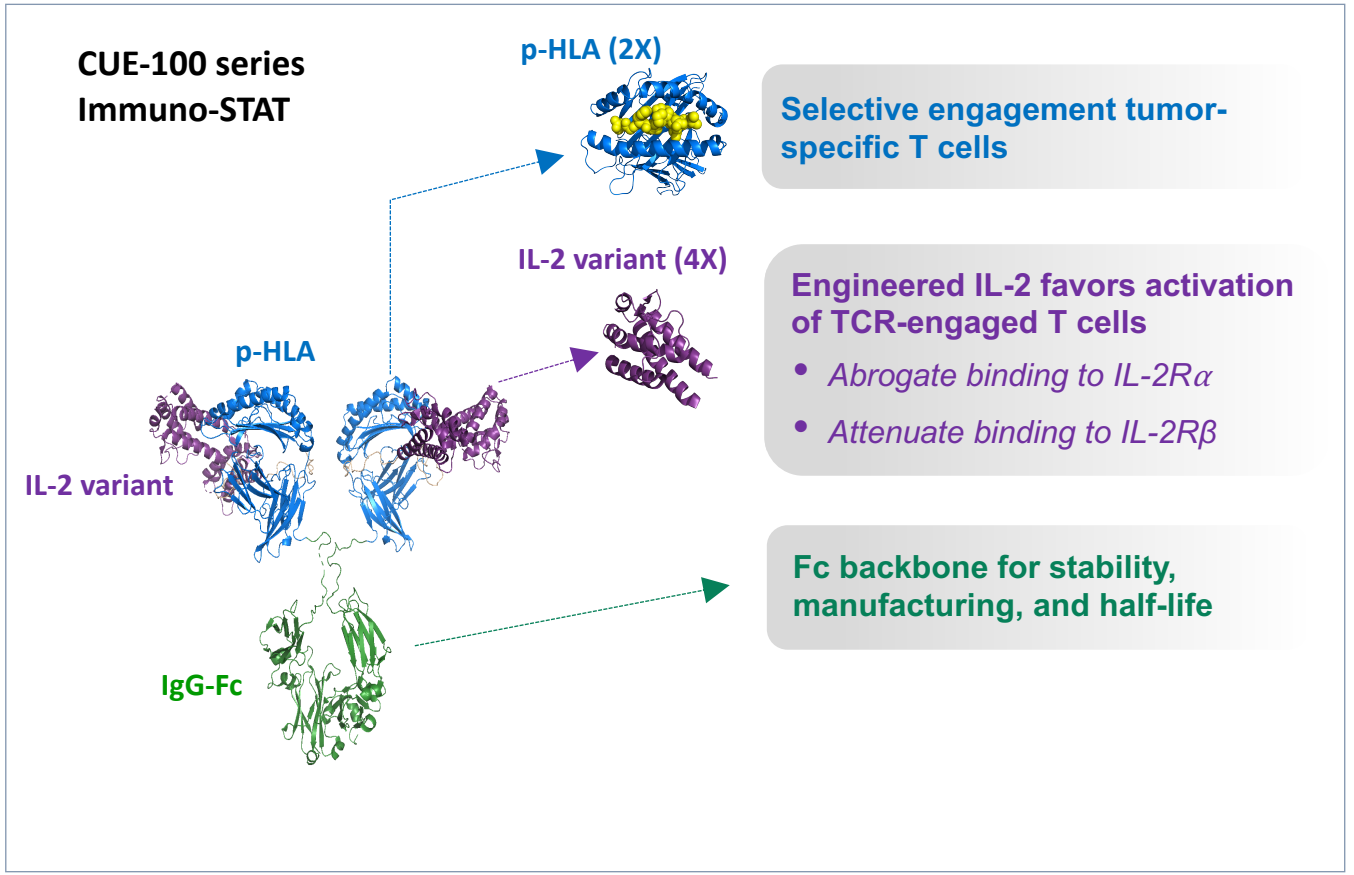
Non-specific Activation of ALL CD8+ T cells



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

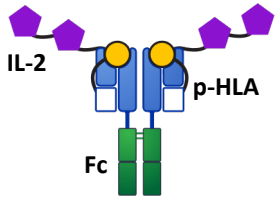




CUE-100 Series: Directing IL-2 Activity to Tumor-specific T cells and Enhancing Tolerability and Efficacy

IL-2 Immuno-STAT

CUE-100 series



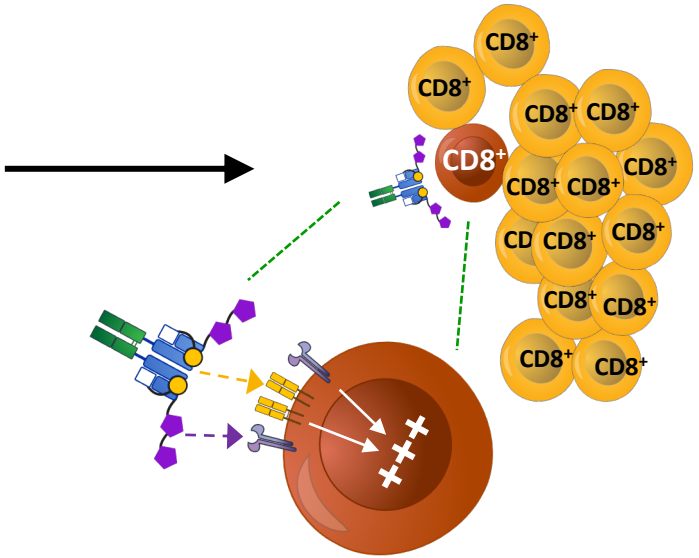
LEGEND

- IL-2
- IL-2R
- Peptide-HLA
- TCR

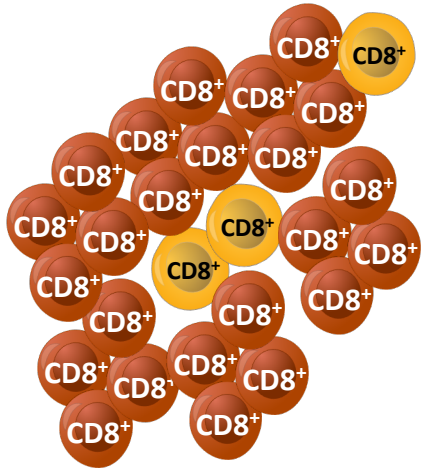
CD8+ TUMOR-SPECIFIC CD8+ T CELL

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)

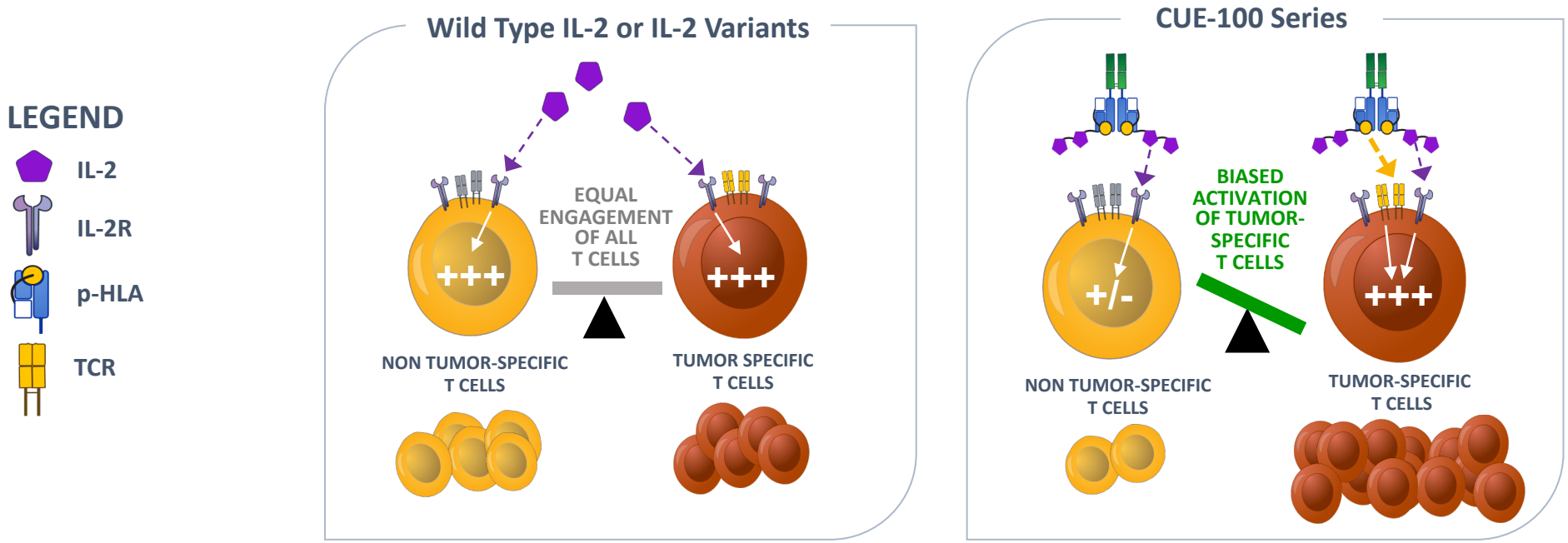


ADVANTAGES

- 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

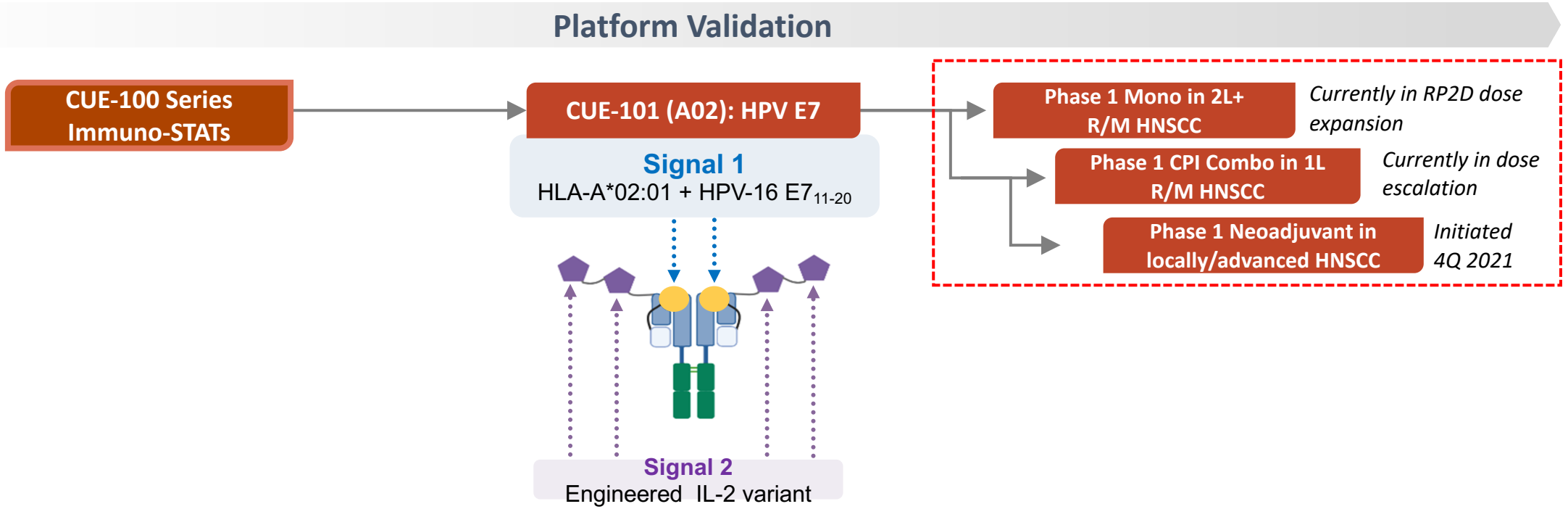
CUE-100 Series: Opportunity to Maximize the Fullest Potential of IL-2

The CUE-100 series has the potential of enabling a broad therapeutic window to enhance IL-2 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*

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

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

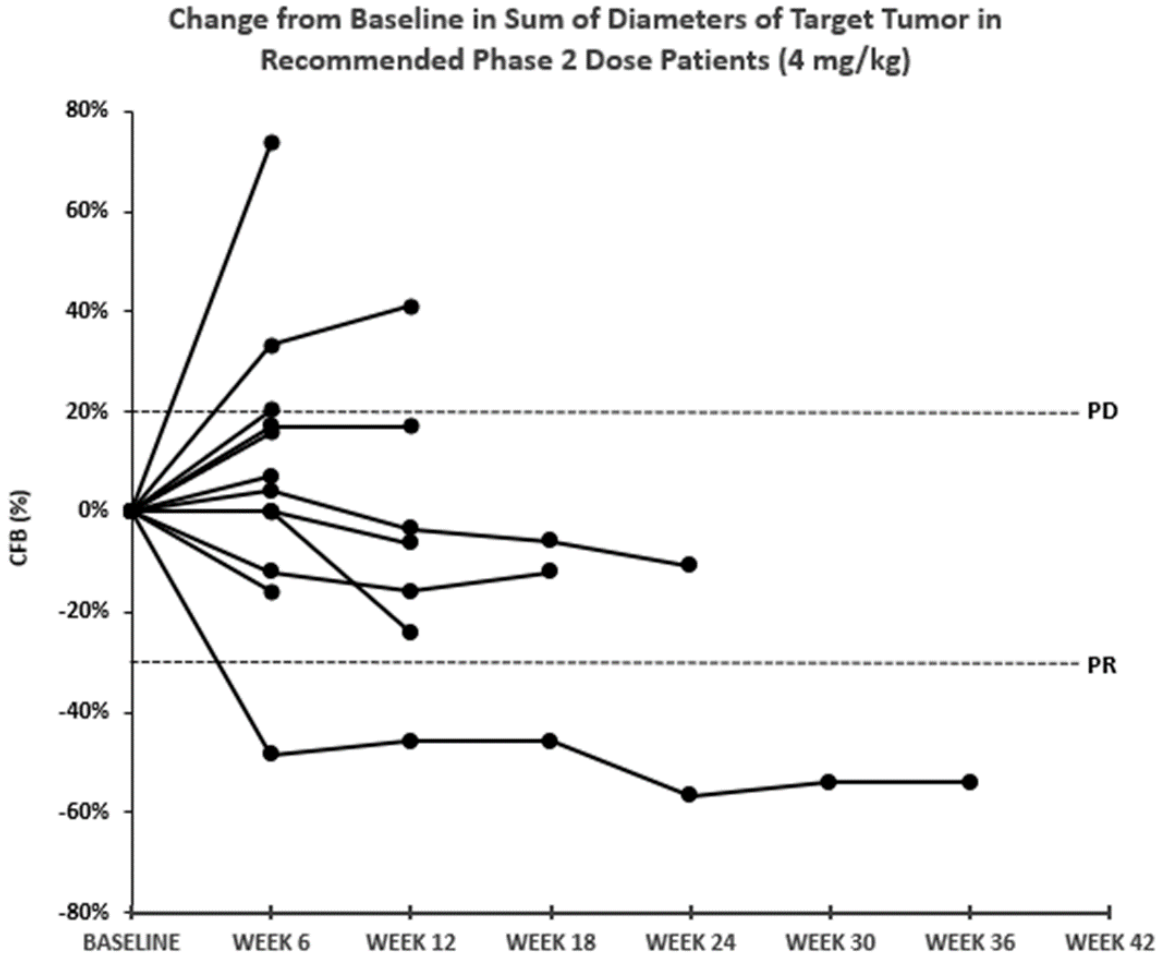
- Patients given CUE-101 doses ranging from 0.06 mg/kg – 8 mg/kg
- Generally well-tolerated with no MTD identified

Efficacy

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

CUE BIOPHARMA

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



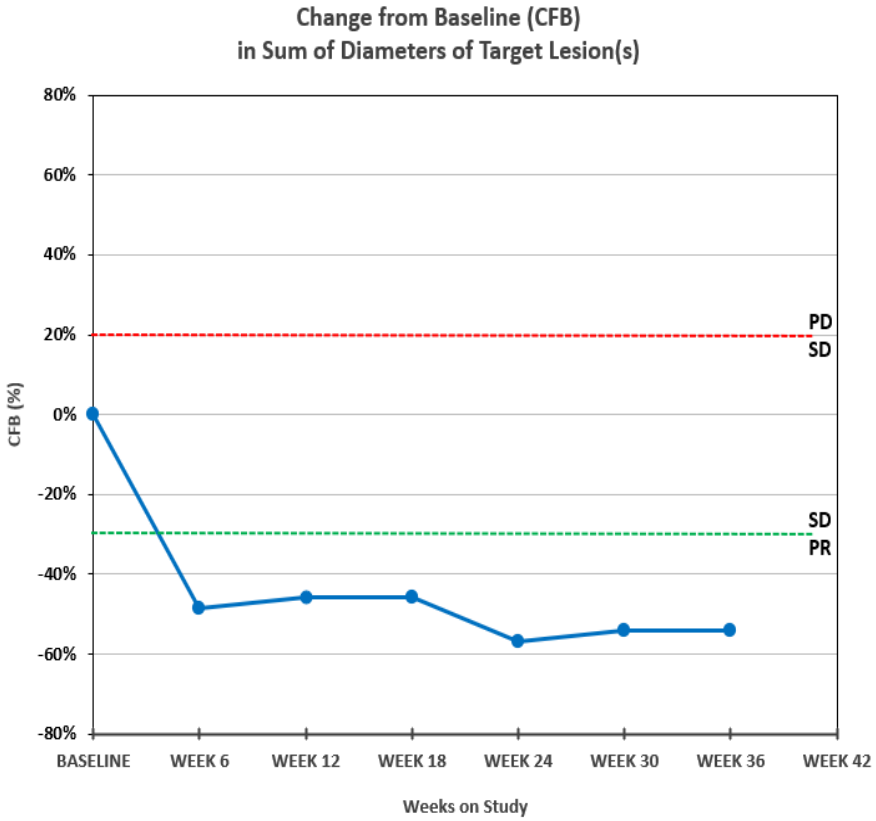
Responses	N	%
Objective Response (CR or PR confirmed ≥ 4 weeks)	1	7.7%
Durable Stable Disease (SD sustained for ≥ 12 weeks*)	5	38.5%
Clinical Benefit (CR/PR + durable SD)	6	46.2%

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.*

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

Case History

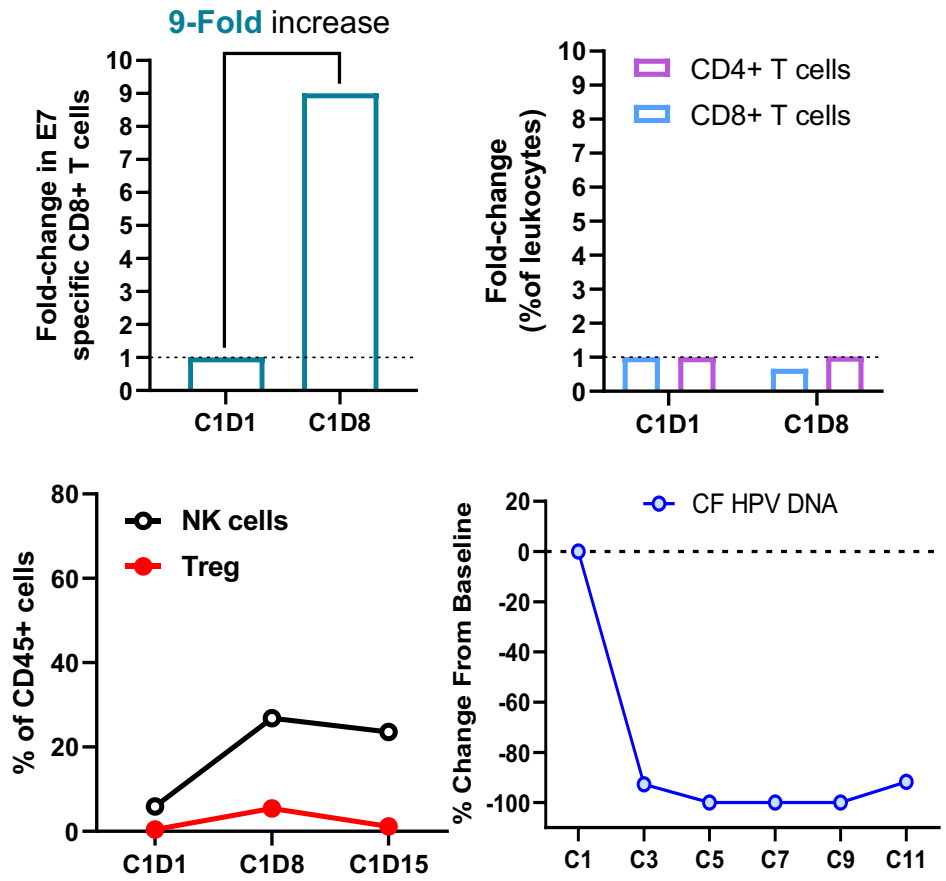
- Prior therapy:
  - 1L cetuximab
  - 2L pembrolizumab
- Progressive disease prior to enrollment
- Treated in metastatic 3L setting with 4.0 mg/kg CUE-101 Q3W (Cohort 6)
- Patient completed 13 cycles of CUE-101 and remains on study with PR ongoing



- 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

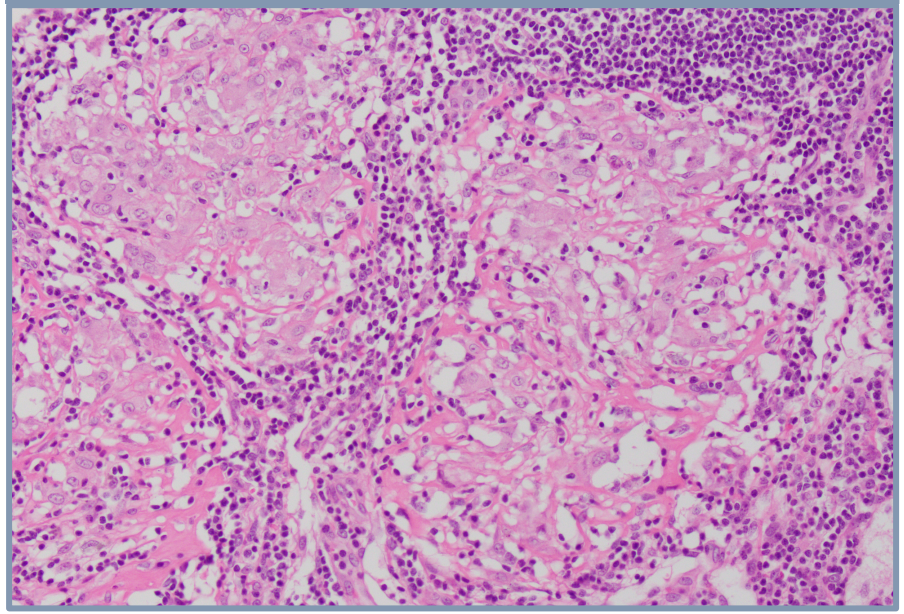


CUE-101: Tumor Necrosis and T Cell Infiltrates in Target Lesions

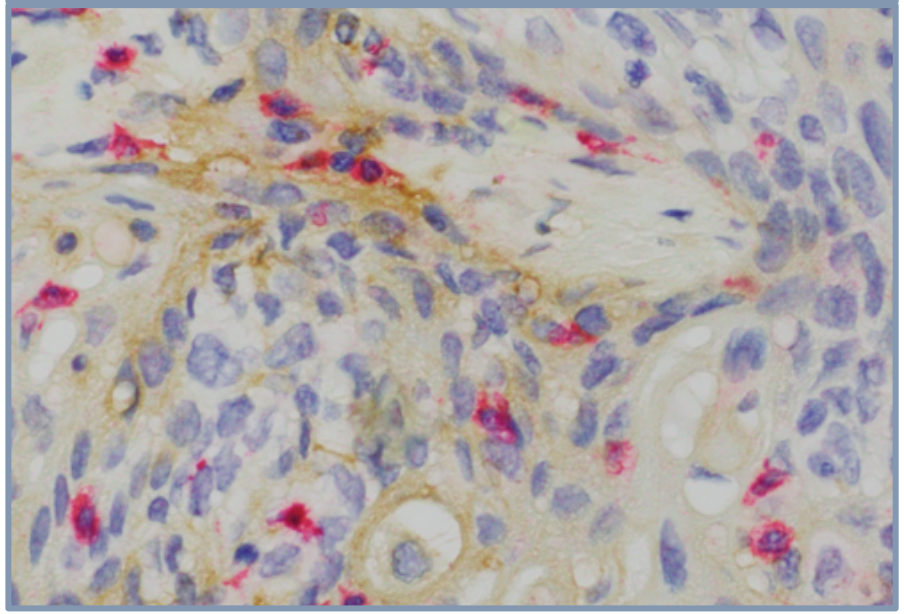
Case History

- 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)



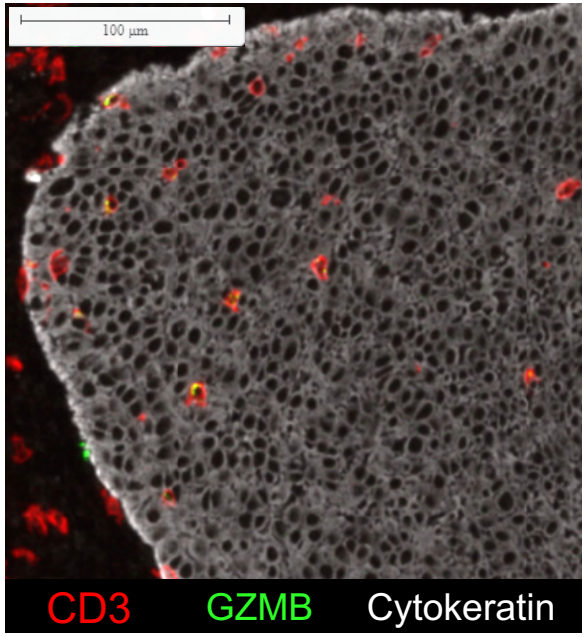
Patient remains disease free post resection

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

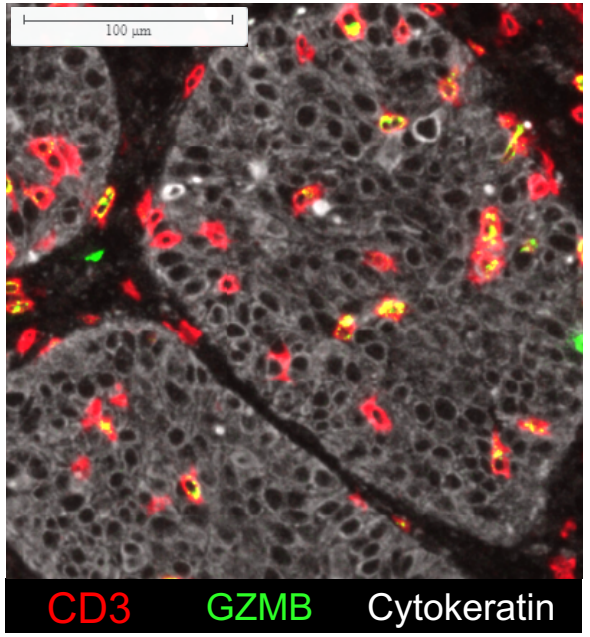
Case History

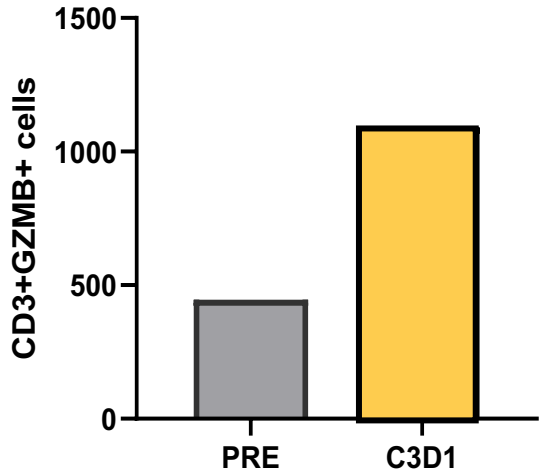
- Prior therapy:
  - 1L chemotherapy
  - 2L pembrolizumab
- Progressive disease prior to enrollment
- Treated in metastatic 3L setting with 2.0 mg/kg CUE-101 Q3W (Cohort 5)

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

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*

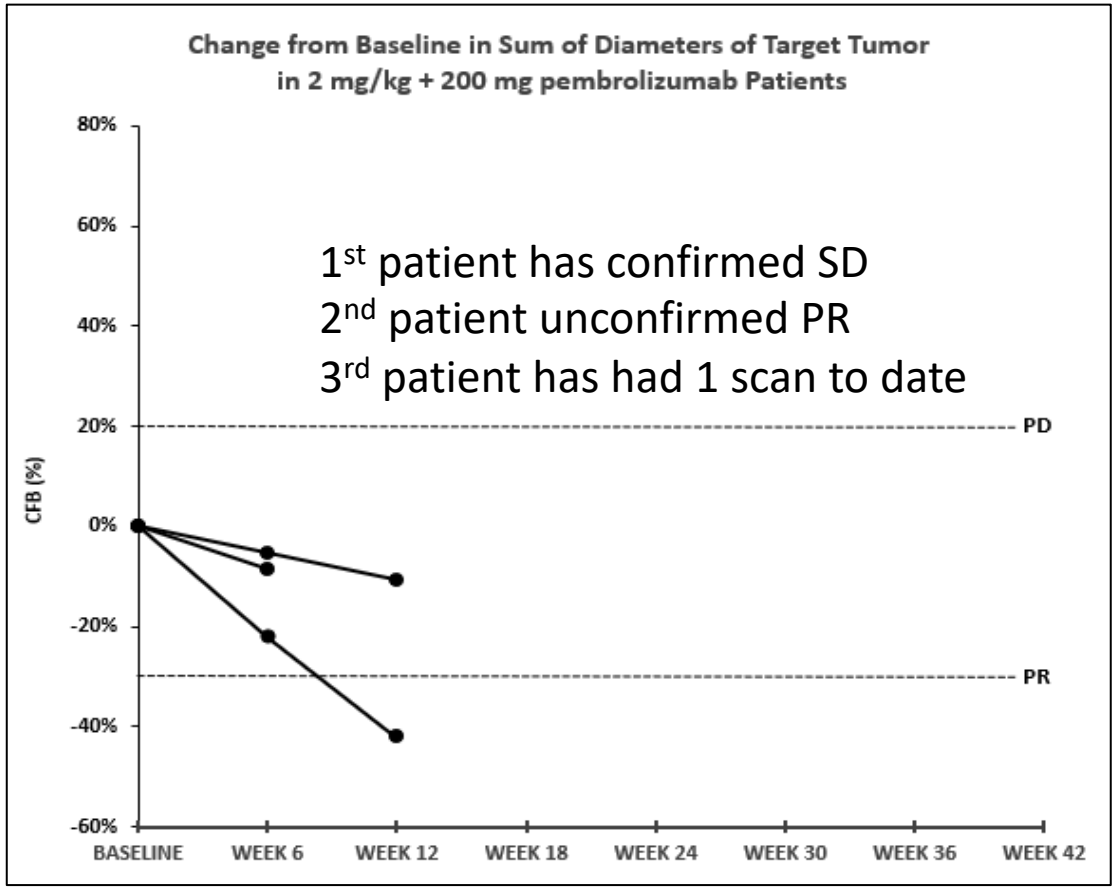
Cohort 2 → *Dosing complete, no DLTs*

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)



CUE-101: Potential for Multiple Registration Paths

Monotherapy

- 2nd line+ therapy for HPV+ head and neck cancer

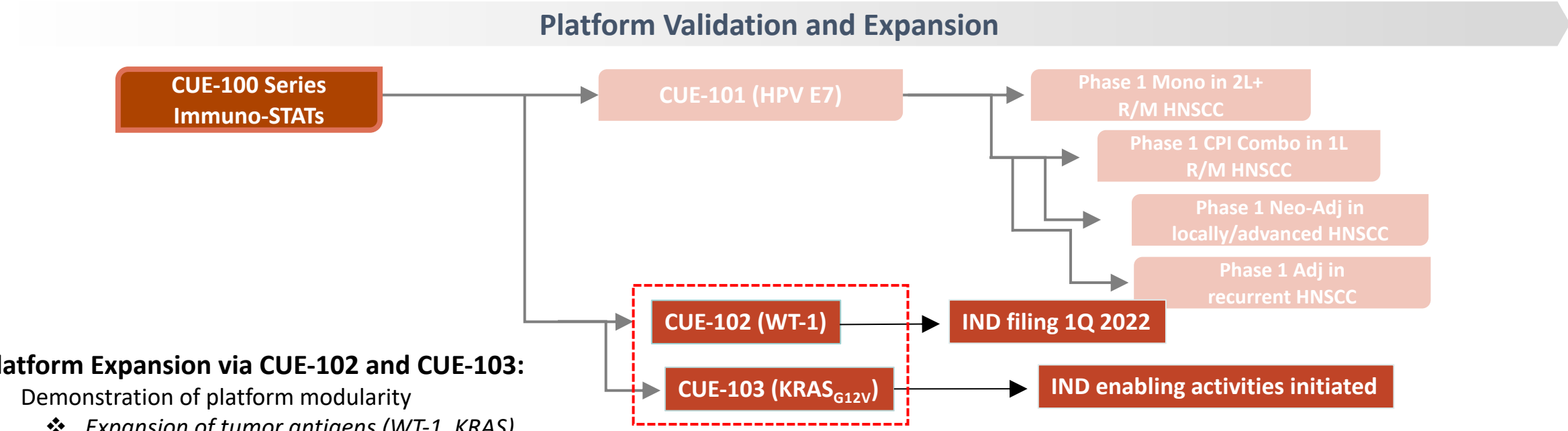
Combination therapy

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

Neoadjuvant therapy

- Early treatment in neoadjuvant setting (study launched in 2H 21)

CUE-100 Series: Validate, Expand and Accelerate

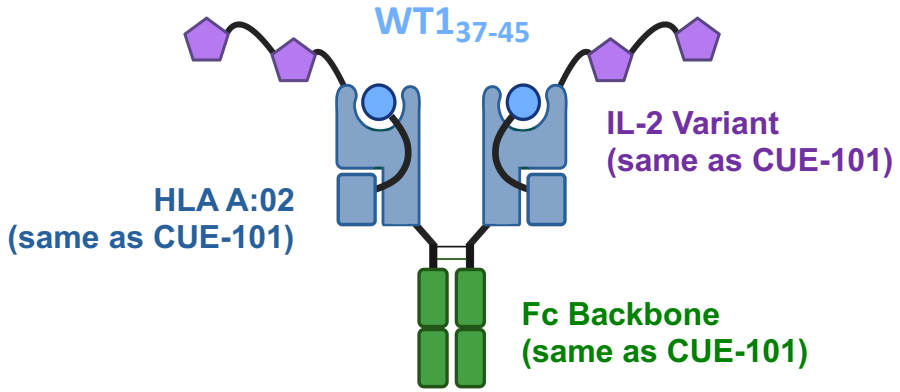


Platform Expansion via CUE-102 and CUE-103:

- ✓ 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*

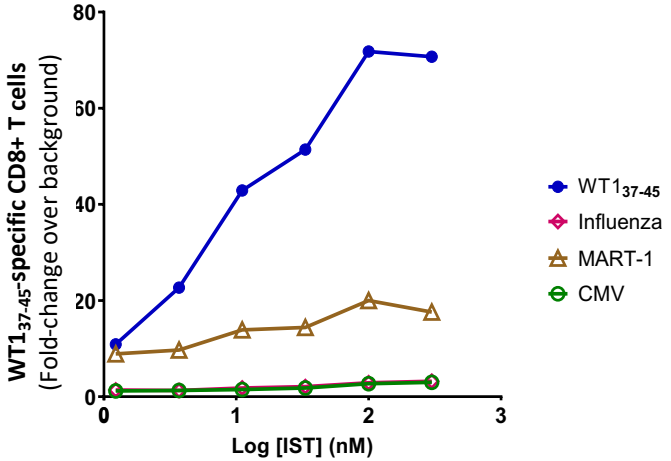
CUE-102: Targeting Wilms Tumor 1 (WT1) – IND Filing 1Q 2022

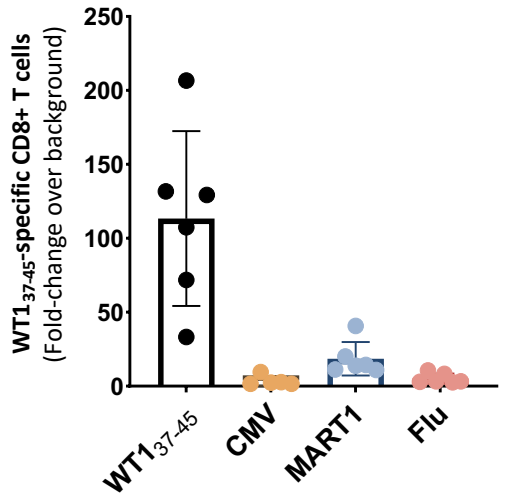
Molecular Design

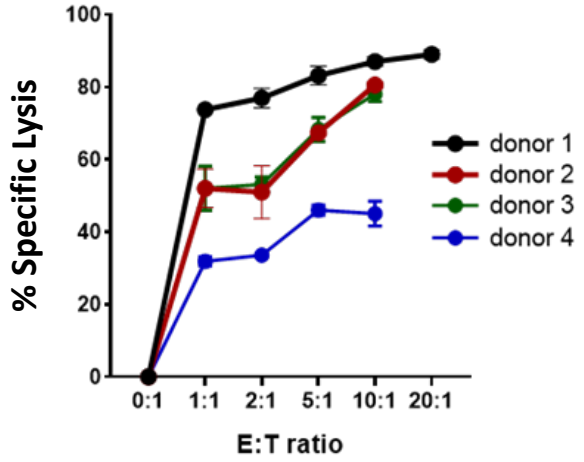


- Top-ranked onco-fetal tumor antigen by the NCI with restricted tissue-expression
- Broad therapeutic opportunity in numerous solid cancers and hematological cancers
- Core IL-2 framework is de-risked by the clinical experience of CUE-101

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



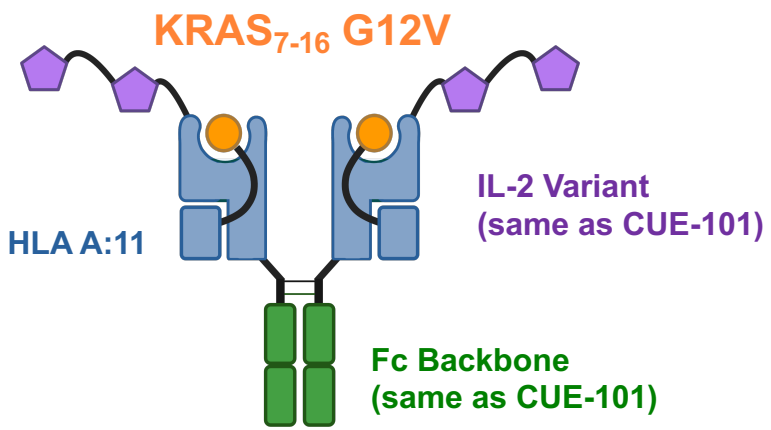




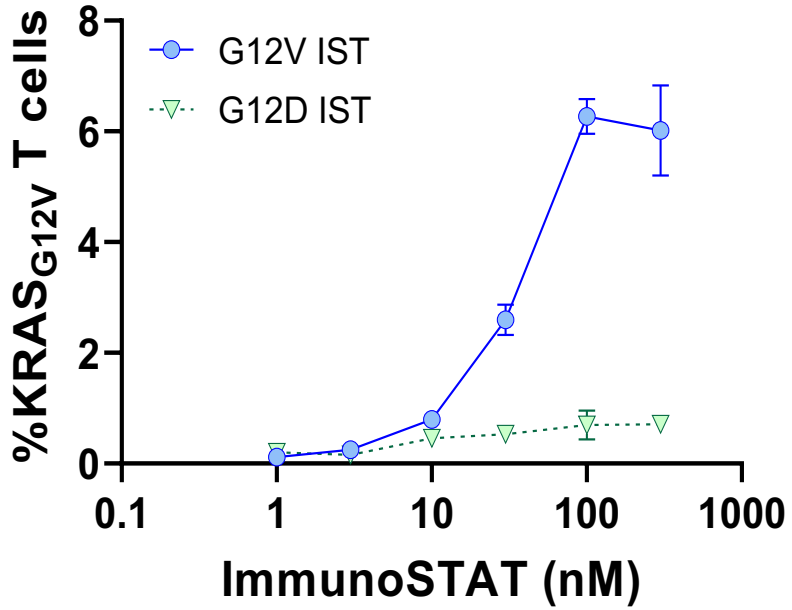
CUE-102 Expands WT-1-specific T Cells that are Cytolytic

CUE-103: KRAS G12V Proof of Concept for Targeting KRAS Mutations

Molecular Design



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

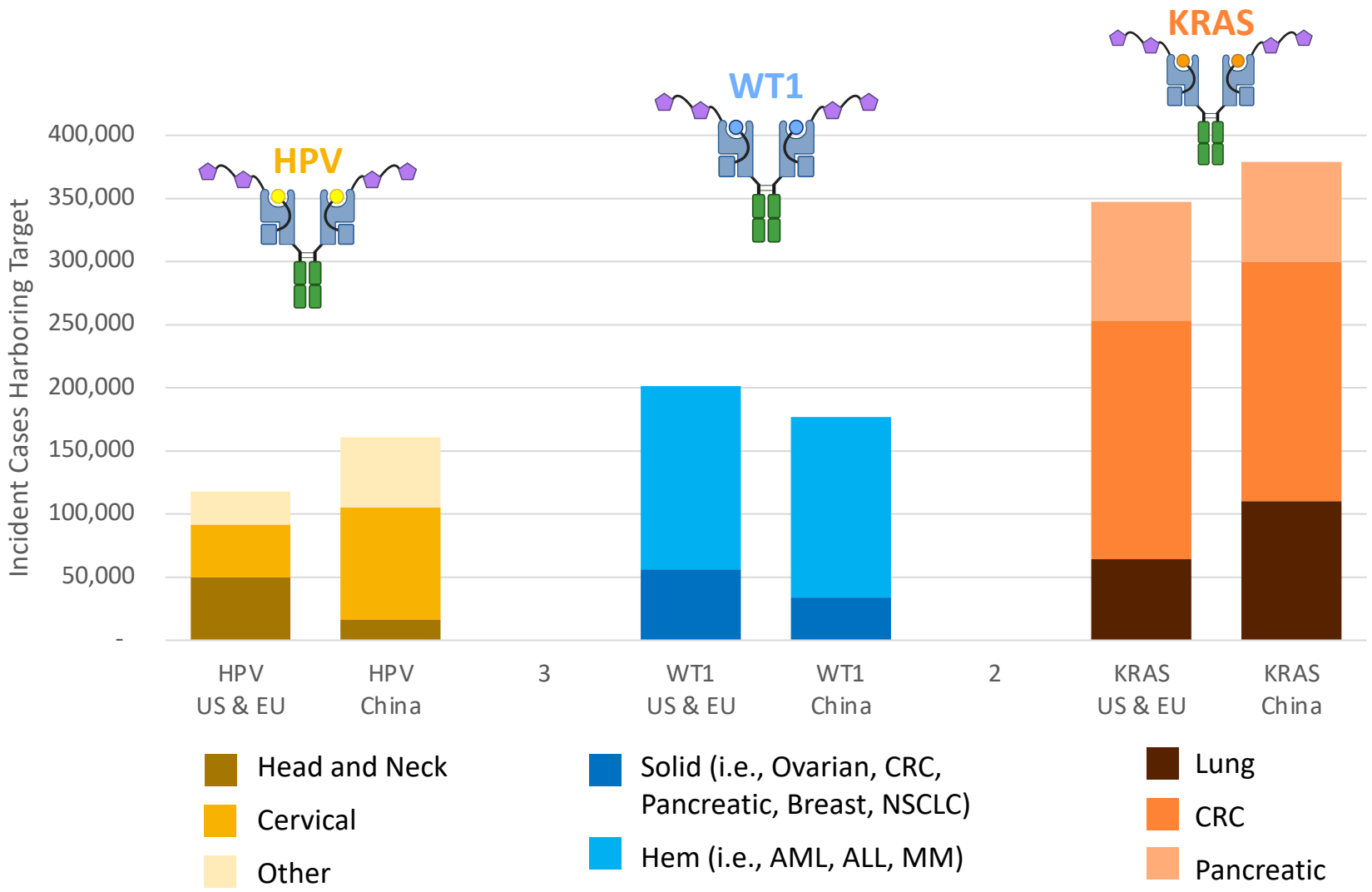


- Broad therapeutic opportunity for targeting of multiple cancers with KRAS driver mutations (NSCLC, CRC, PC, etc.)
- $KRAS_{G12V}$ is a key driver mutation in highly prevalent solid tumors
- $KRAS_{G12V}$ is a validated epitope that is recognized by anti-tumor T cells
- $KRAS_{G12V}$ A11 asset serves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

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

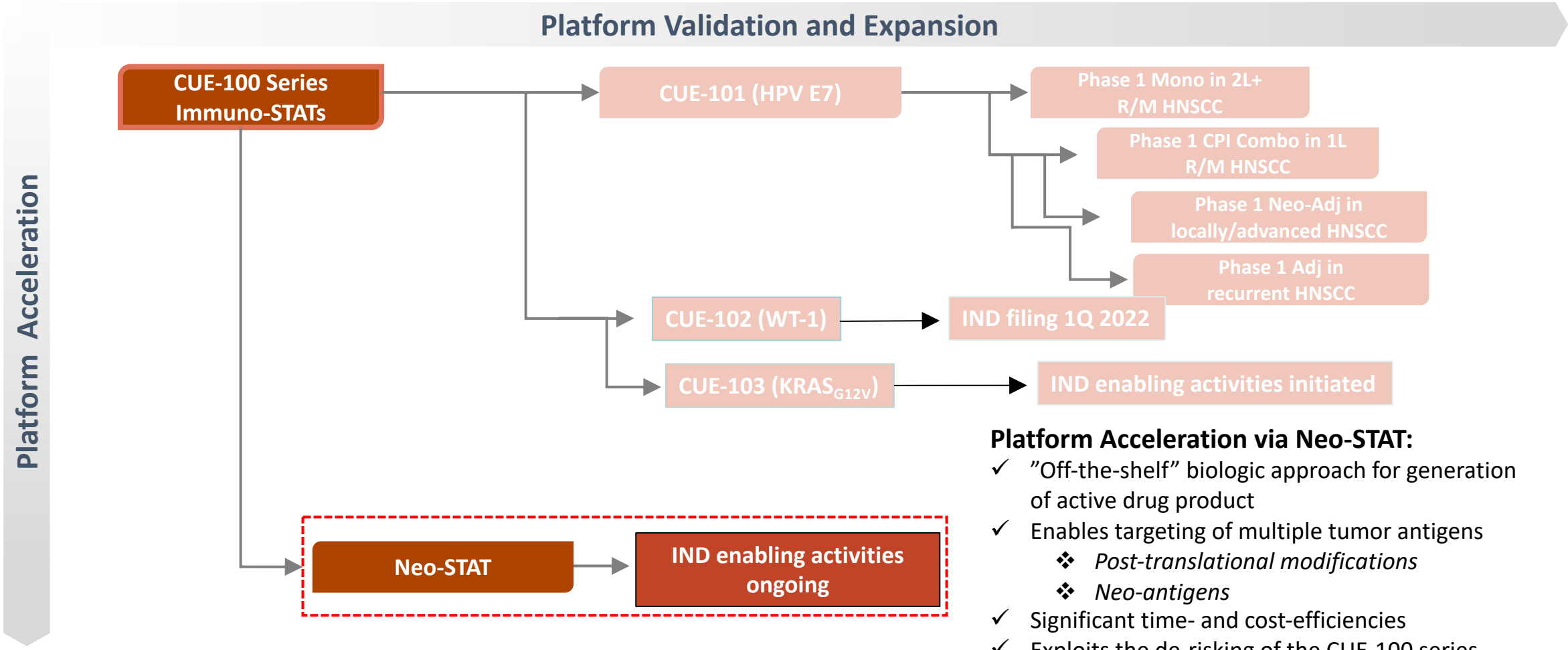
Broad Universe of Addressable TCR Targets with CUE-100 Series

- 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

CUE-100 Series: Validate, Expand and Accelerate



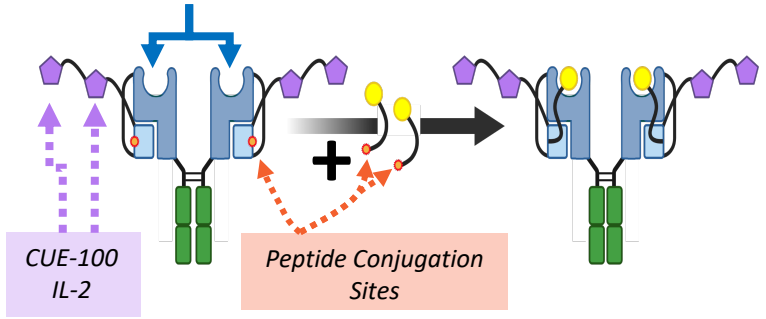
Platform Acceleration via Neo-STAT:

- ✓ "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*

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

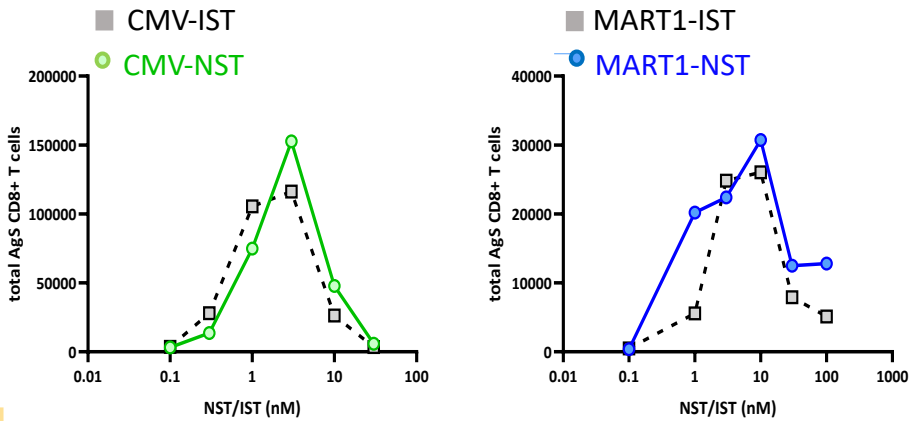
Empty HLA
Stabilized through engineering

Neo-STAT
Rapid conjugation of tumor epitopes

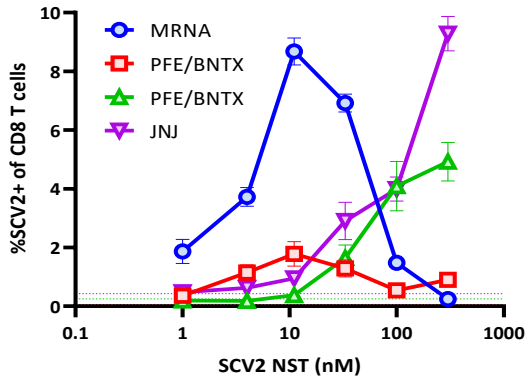


Neo-STAT Manufacturability	HLA-A02	HLA-A11	HLA-A24
Production	✓✓	✓✓	✓✓
Biophysical Properties	✓✓	✓✓	✓✓
Biological Activity	✓✓	✓✓	Ongoing
Initiation of CMC to support IND	✓✓	TBD	TBD

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



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



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**

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

Thank you

Rationally Engineered Biologics to Restore Immune Balance by Harnessing Nature's Cues for Selective and Specific Immune Modulation

CUE™ BIOPHARMA