



# THE POWER OF tomorrow

Engaging the TCR to Transform  
the Treatment of Solid Tumors

**Corporate Presentation**

October 2022

**TCR<sup>2</sup>**  
THERAPEUTICS

# Forward Looking Statements

This presentation has been prepared by TCR<sup>2</sup> Therapeutics Inc. (“we,” “us,” or “our”) and contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our clinical results and other future conditions. All statements, other than statements of historical facts, contained in this presentation, including express or implied statements regarding our expectations for the Phase 2 clinical trial of gavo-cel and the Phase 1/2 clinical trial of TC-510, including expected progress and timing of updates; our expectations for the safety and efficacy of, and enhancements to, gavo-cel, TC-510 and our other product candidates including compared to other T-cell therapy approaches; our expectations regarding the estimated patient populations and related market opportunities in gavo-cel’s, TC-510’s and our other product candidates’ targeted indications; our expectations regarding manufacturing of gavo-cel, TC-510 and our other product candidates; our expectations regarding our development programs and IND-enabling studies; our expectations regarding expansion opportunities for our TRuC platform; and our expectations regarding our financial position are forward-looking statements. These statements are based on management’s current expectations and beliefs and are forward-looking statements which involve risks and uncertainties that could cause actual results to differ materially from those discussed in such forward-looking statements.

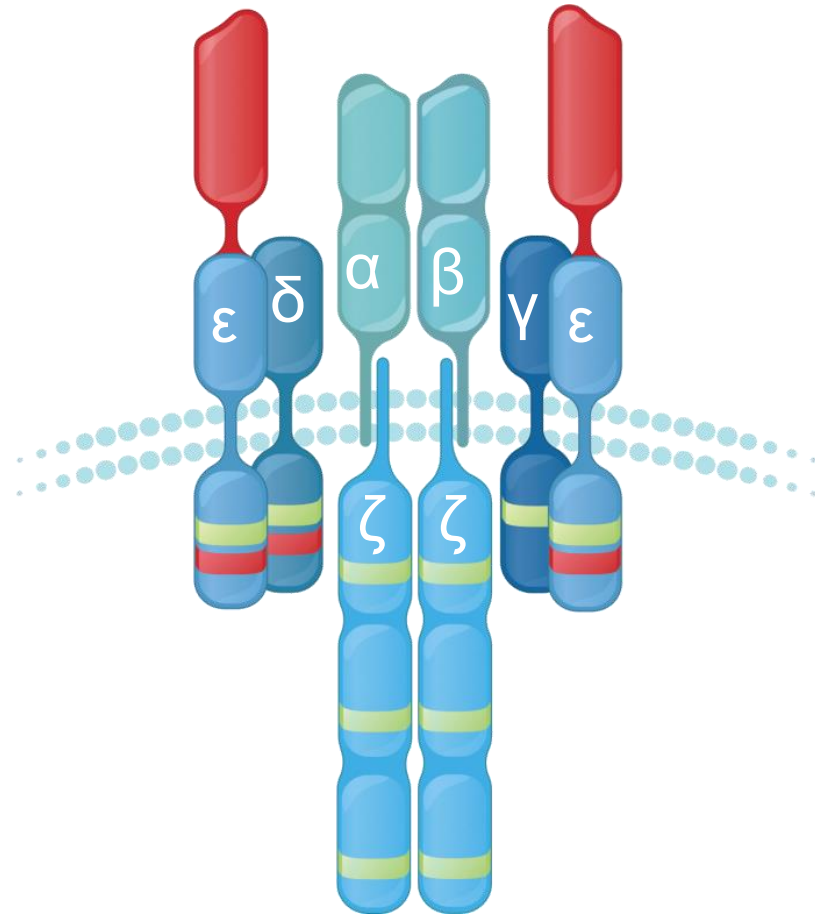
Such risks and uncertainties include, among others: uncertainties inherent in clinical studies and in the availability and timing of data from ongoing clinical studies; whether interim results from a clinical trial will be predictive of the final results of a trial; the possibility that positive results from preclinical studies and correlative studies may not necessarily be predictive of the results of our planned clinical trials, including the Phase 2 clinical trial of gavo-cel and Phase 1/2 clinical trial of TC-510; the risk that the results from

the Phase 2 clinical trial of gavo-cel and Phase 1/2 clinical trial of TC-510 will not support further development and marketing approval; the risk that we may be unable to gain approval of gavo-cel, TC-510 and our other product candidates on a timely basis, if at all; the risk that we have over-estimated the potential patient population for our product candidates, if approved; the risk that the current COVID-19 pandemic will impact our clinical trials and other operations; and the other risks set forth under the caption “Risk Factors” in our most recent Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the SEC on March 22, 2022, as updated in our most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, as filed with the SEC on November 8, 2022, and in our future filings with the SEC available at the SEC’s website at [www.sec.gov](http://www.sec.gov). New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. You should not place undue reliance on any forward-looking statements, which speak only as of the date they are made.

While we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.



# Innovating the Natural Power of the TCR for Solid Tumors



**TRuC® Platform**  
(T Cell Receptor Fusion Construct)

## We Are Solving the Translation of Cell Therapies to Solid Tumors with a New Modality: **TRuC-T Cells**

- ✓ Comprehensive T cell activation through **integration with full TCR complex**
- ✓ **No HLA restriction** supports broad patient access
- ✓ **Versatile platform** with flexibility to add enhancements
- ✓ **Multiple high-value indications** across oncology and autoimmune

# Refocused Pipeline to Deliver Near-Term Clinical Data

Program	Indication(s)	Target	Enhancement / Combo	Discovery	Lead Optimization	IND Enabling	Phase 1	Phase 2	Phase 3
<b>Oncology</b>									
<b>gavo-cel</b>	Ovarian cancer (Treating)	MSLN	Checkpoint inhibitor						
<b>gavo-cel</b>	MPM (Treating)	MSLN	Checkpoint inhibitor						
<b>gavo-cel</b>	NSCLC (Enrolling)	MSLN	Checkpoint inhibitor						
<b>gavo-cel</b>	Cholangiocarcinoma (Next wave)	MSLN	Checkpoint inhibitor						
<b>TC-510</b>	Ovarian cancer, MPM, Pancreatic, Colorectal, TNBC	MSLN	PD-1 switch						
<b>TC-520</b>	RCC, AML	CD70	IL-15						



# Leading the Way with gavo-cel

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*Stage of Development: Phase 2*

# Significant Potential Opportunity in Mesothelin-Expressing Solid Tumors

~215,000 Patients Across Multiple Target Indications

## Mesothelioma

Population: 1,800

- ✓ Orphan Drug Designation
- ✓ 4 RECIST Partial Responses
- ✓ 21/22 Tumor Regression
- ✓ ORR 21%

## NSCLC

Population: 62,600

## Cholangiocarcinoma

Population: 4,000

- ✓ Orphan Drug Designation
- ✓ 1 Partial Response (by Investigator Assessment)
- ✓ 1/1 Tumor Regression

## Ovarian Cancer

Population: 12,400

- ✓ 2 RECIST Partial Responses
- ✓ 6/7 Tumor Regression
- ✓ ORR 29%

## Esophageal Cancer

Population: 5,000

## Triple Negative Breast Cancer

Population: 15,000

## Pancreatic Cancer

Population: 38,000

## Gastric Cancer

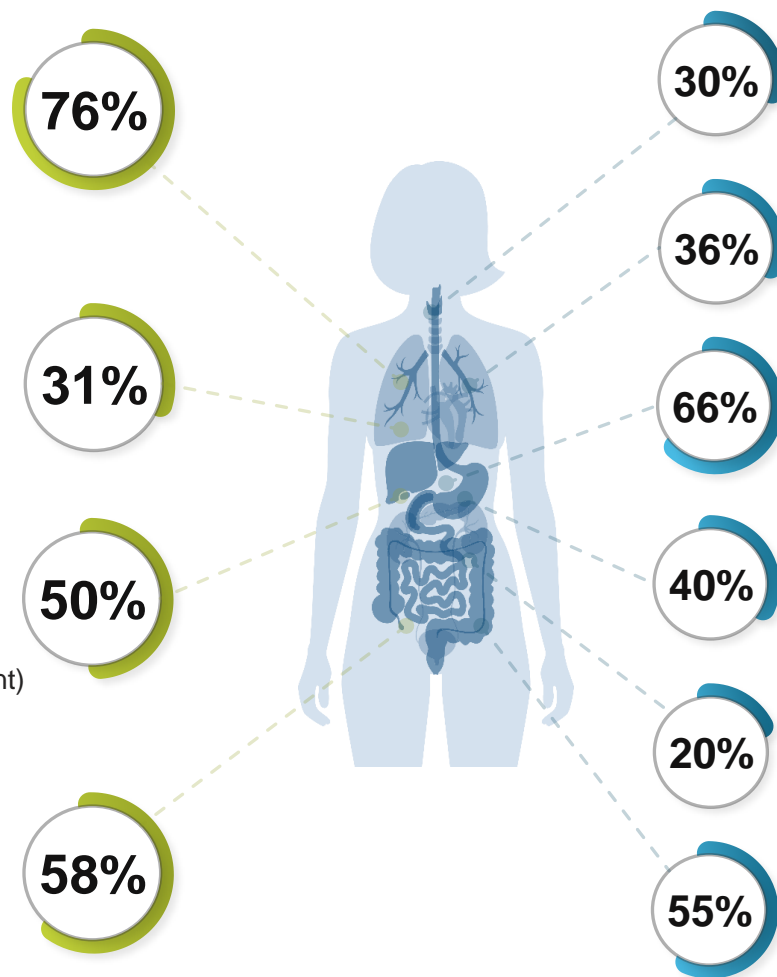
Population: 11,000

## Endometrial Cancer

Population: 13,000

## Colorectal Cancer

Population: 81,000



Percent of Patients with Mesothelin Surface Expression

NSCLC, Non-Small Cell Lung Cancer; ORR, Overall Response Rate  
Refs: Inaguma 2017, SEER Statistics, Morello 2016, Tozbiakian 2014

# Phase 1 Key Takeaways

## Efficacy Data

- 93% - Heavily pretreated patients that experienced tumor regression
- 77% - Disease Control Rate (DCR)
- New RECIST Responses in ovarian cancer (29% ORR), MPM (21% ORR)
- MPM: 5.6 PFS, 11.2 OS

## Safety Data

- RP2D: manageable safety profile and reversible adverse events
- Most frequent Grade  $\geq 3$  AE: CRS in 15% of patients

## Path Forward

- Ovarian Cancer: earlier focus due to encouraging early activity
- MPM: potential frontline setting if CPI combo improves durability of benefit
- NSCLC: expansion opportunity with new MSLN threshold

## Baseline Established

Additional strategies in the Phase 2 clinical trial are designed to improve preliminary profile

- ✓ Combination with checkpoint inhibitors
  - ✓ Redosing
  - ✓ Earlier lines of therapy

# Grade $\geq 3$ Treatment Emergent Adverse Events

				RP2D				
Adverse Event	DL 0 (no LD) 5x10 <sup>7</sup> /m <sup>2</sup> n=1 (%)	DL 1 5x10 <sup>7</sup> /m <sup>2</sup> n=8 (%)	DL 2 (no LD) 1x10 <sup>8</sup> /m <sup>2</sup> n=1 (%)	DL 3 1x10 <sup>8</sup> /m <sup>2</sup> n=13 (%)	DL 3.5 3x10 <sup>8</sup> /m <sup>2</sup> n=5	DL 4 (no LD) 5x10 <sup>8</sup> /m <sup>2</sup> n=1 (%)	DL 5 5x10 <sup>8</sup> /m <sup>2</sup> n=3 (%)	Overall n=32 (%)
<i>Hematologic</i>								
Lymphopenia	0	8 (100)	0	13 (100)	5 (100)	0	3 (100)	29 (91)
Neutropenia	1 (100)	8 (100)	0	13 (100)	5 (100)	1 (100)	3 (100)	31 (97)
Thrombocytopenia	0	2 (25)	0	2 (15)	1 (20)	0	2 (67)	7 (22)
<i>On Target / On Tumor</i>								
CRS	0	2 (25)	0	2 (15)	1 (20)	0	3 (100)	8 (25)
HLH/ MAS	0	0	0	0	0	0	0	0
Neurotoxicity	0	0	0	0	0	0	0	0
<i>On Target / Off Tumor</i>								
Pericarditis / Pericardial effusion	0	0	0	0	1 (20)	0	0	1 (3)
Pleuritis / Pleural effusion	0	0	0	1 (8)	1 (20)	0	0	2 (6)
Peritonitis / Ascites	0	0	0	1 (8)	0	0	0	1 (3)
<i>Other</i>								
Pneumonitis	0	1 (13)*	*0	0	3 (60)	0	1 (33)	5 (16)
Sepsis	0	1 (13)	0	0	0	0	0	1 (3)
Hemorrhage	0	0	0	0	0	0	1 (33)*	1 (3)

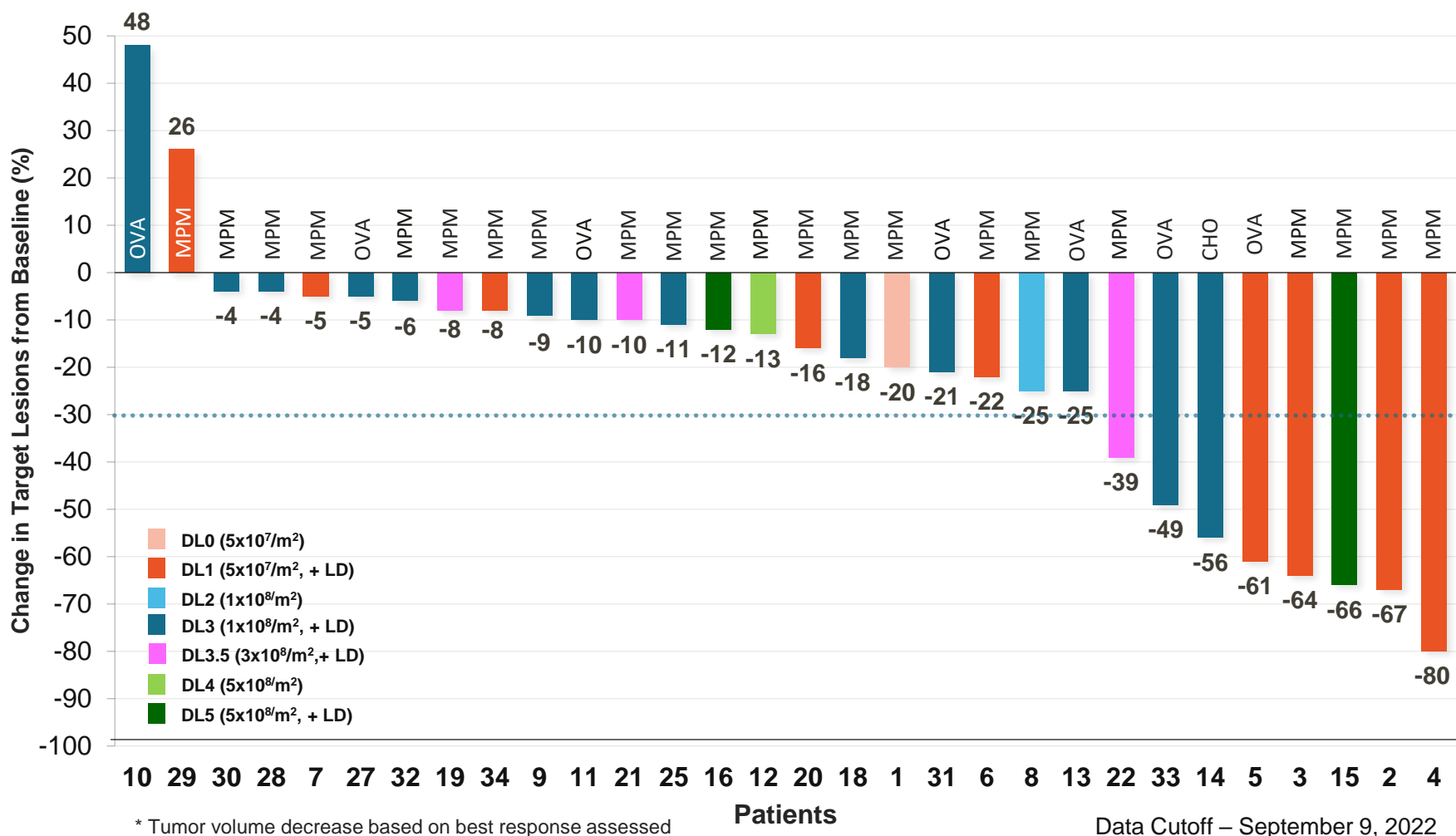
\*Dose Limiting Toxicity

Data Cutoff – September 9, 2022



# Consistent Tumor Regression in Patients with gavo-cel

Tumor Regression in 93% of Patients, Disease Control Rate 77%



## Blinded Independent Central Review

	All	gavo-cel + LD
ORR	20%	22%
MPM ORR	18%	21%
Ovarian ORR	29%	29%

DCR = PR or SD lasting at least 3 months

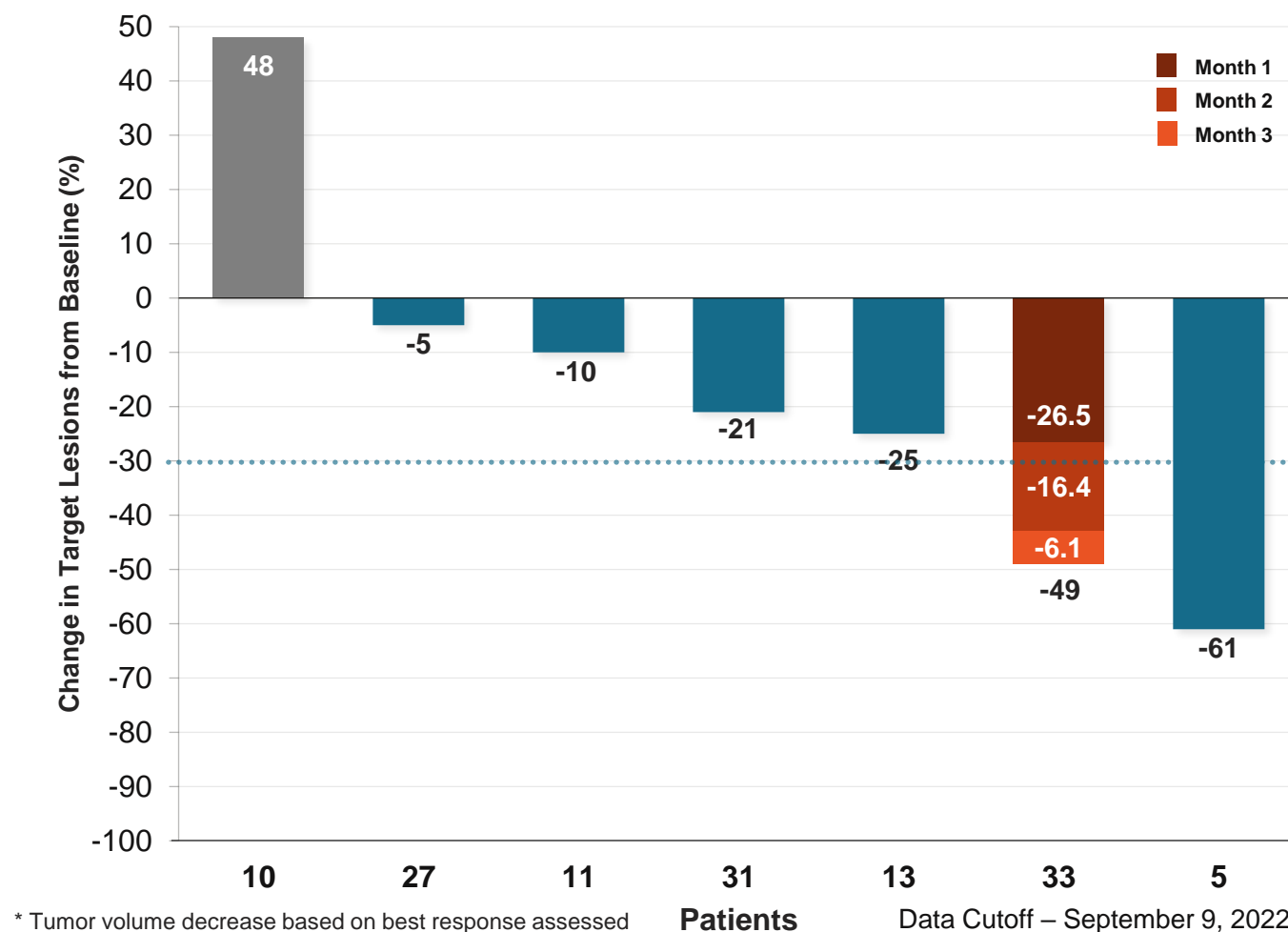
# Promising Signal in Platinum Refractory Ovarian Cancer

## Ovarian Highlights

- 6/7 patients experienced tumor regression
- 2/7 patients experienced RECIST partial responses
- Most recent RECIST response (Patient 33) is ongoing at month 4; experiencing continuous monthly improvement of radiological response

## Efficacy Data

- ORR: 29% (gavo-cel + LD)
- PFS: 5.8 months
- OS: 8.1 months



# Patient 33 – Platinum Refractory Ovarian Cancer

*Partial Response (RECIST v1.1), Tumor Regression Deepened Over 3 Months (49%)*

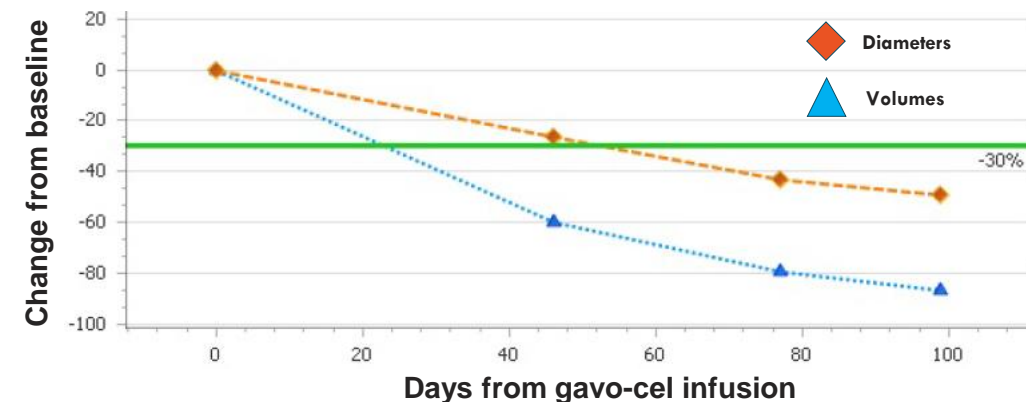
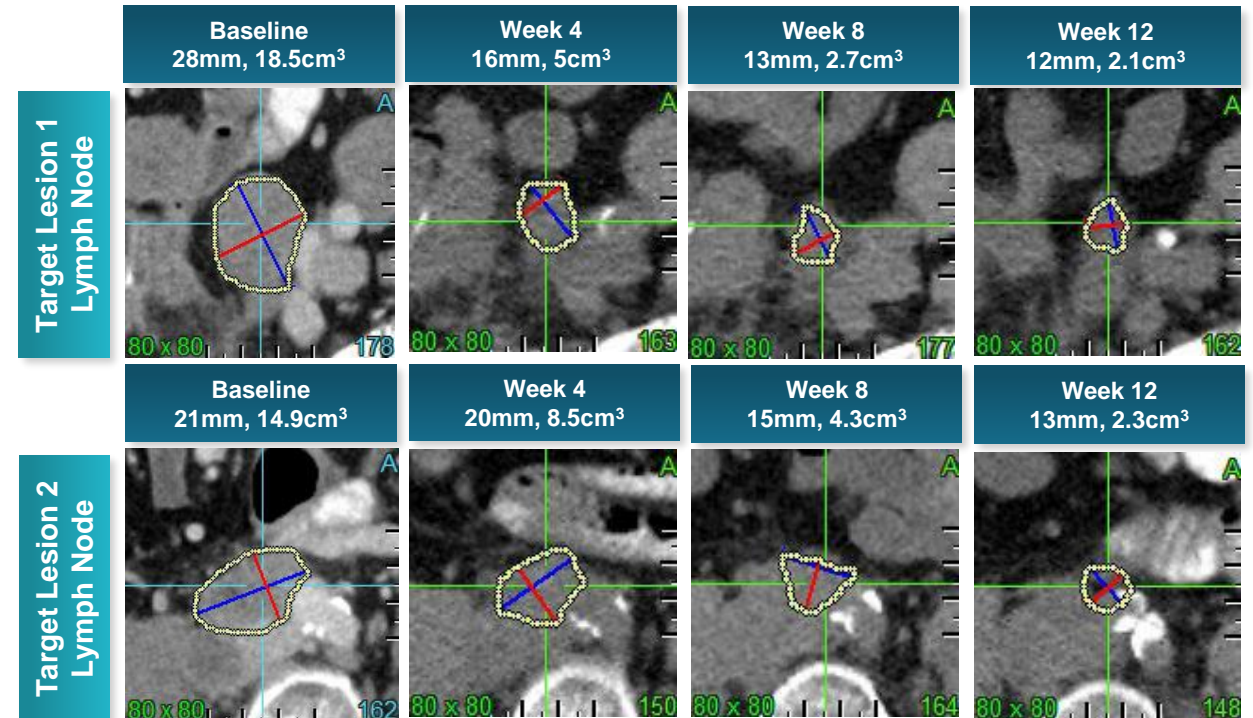
**66-year-old female,**

**High grade, Stage IV serous ovarian cancer**

- *TP53 mutated*
- Total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy
- Carboplatin/paclitaxel
- Bevacizumab/Paclitaxel
- Bevacizumab maintenance
- Weekly Paclitaxel

**Enrolled in gavo-cel Clinical Trial**

- Lymphodepletion with Flu/Cy
- gavo-cel at  $1 \times 10^8/\text{m}^2$  (RP2D)



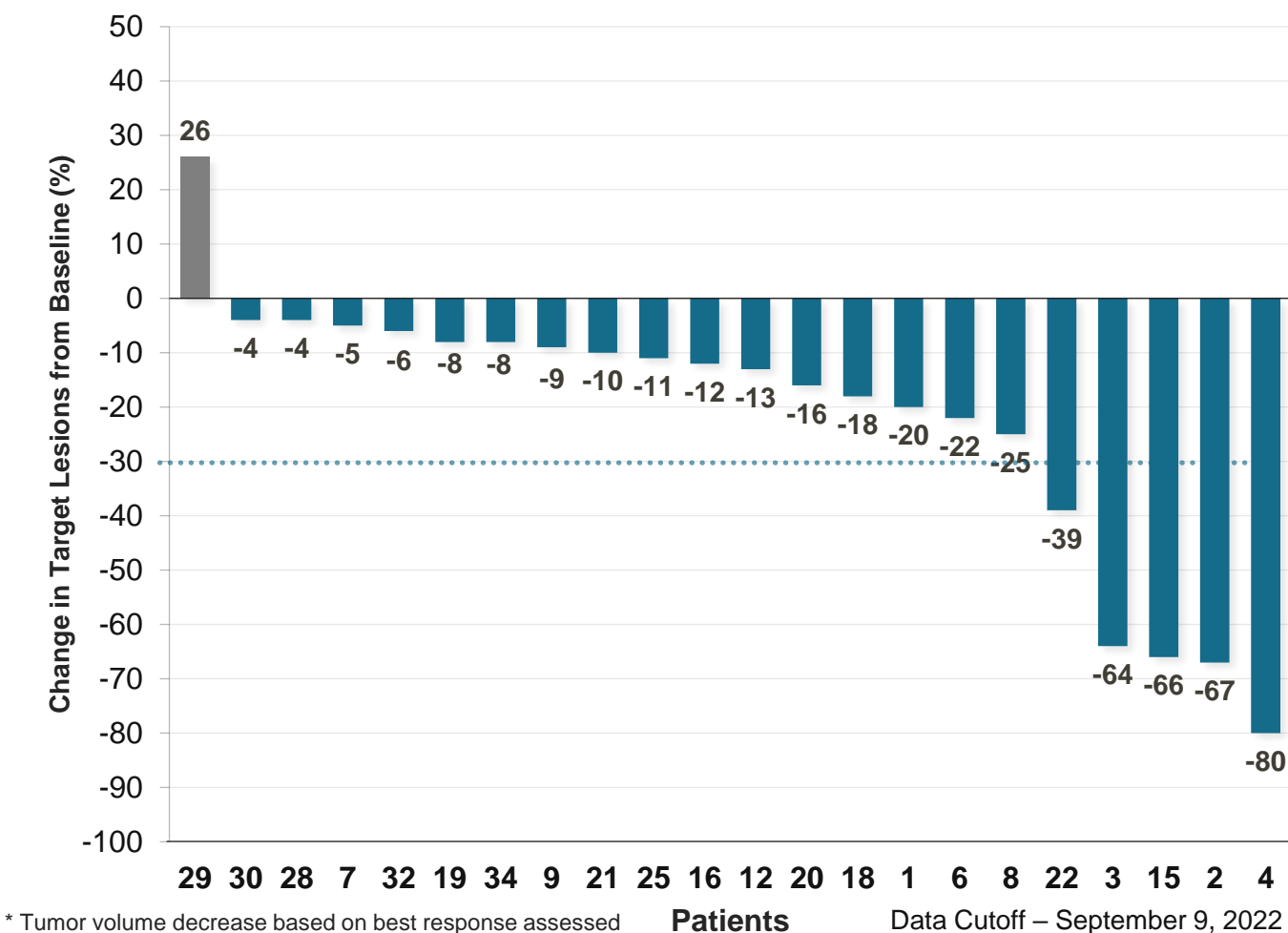
# Phase 1 Data Support a Path Forward as Mesothelioma Leader

## MPM Highlights

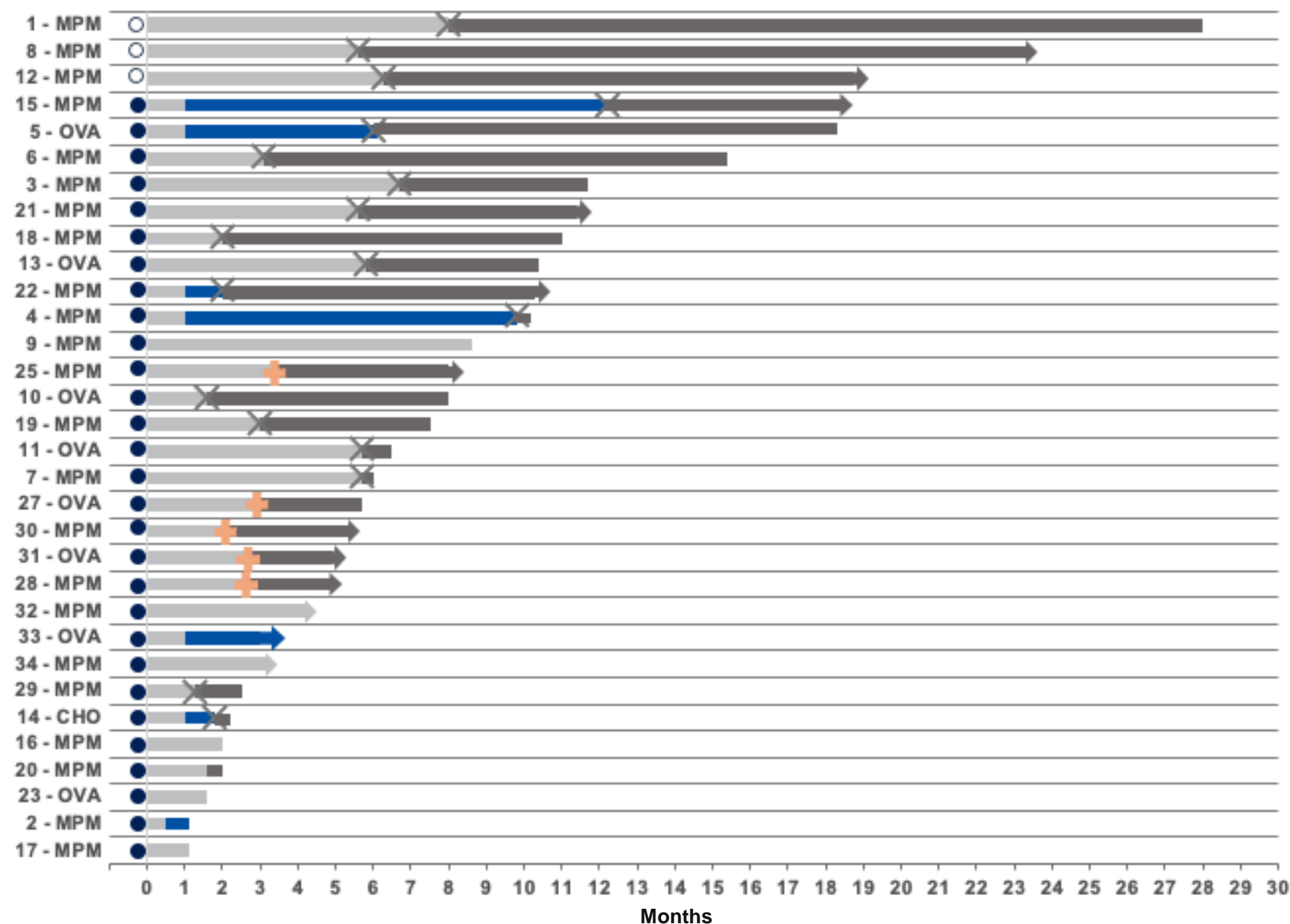
- 21/22 patients experienced tumor regression
- 5/22 patient partial responses by target lesion assessment; 4/22 experienced RECIST partial responses
- 1 patient experienced complete metabolic response

## Efficacy Data

- ORR: 21% (gavo-cel + LD)
- PFS: 5.6 months
- OS: 11.2 months



# Patient Response and Follow-up as of September 9<sup>th</sup>, 2022



**Patients alive at 6 months \*** 70%

**Patients alive at 1 year \*** 31%

**Patients alive as of cutoff** 12

Data Cutoff – September 9, 2022

\*Kaplan-Meier survival estimates

\*\* CHO PR by Investigator Assessment

**Lymphodepletion:** ● LD ○ No LD

**Response:** ■ SD ■ PR ■ CR × PD

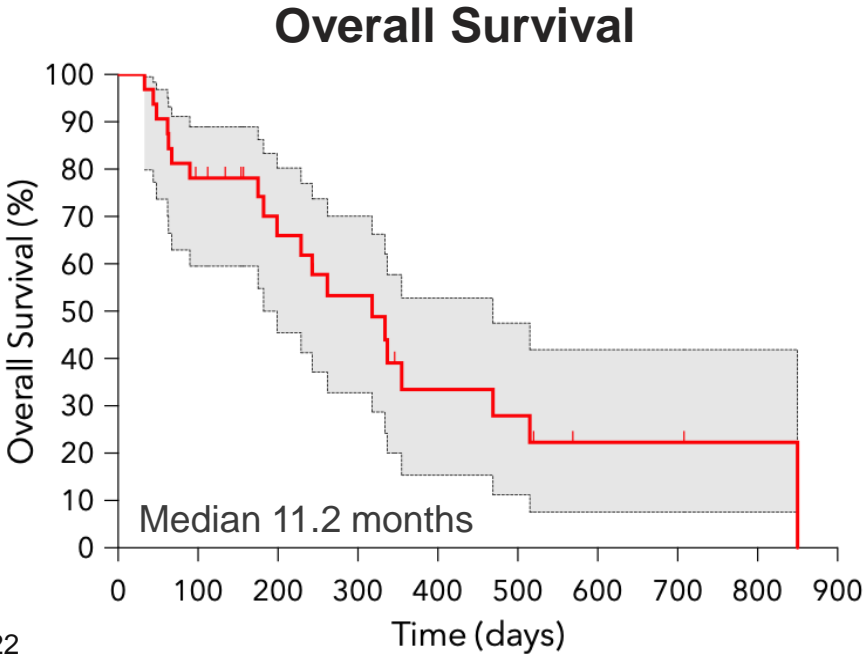
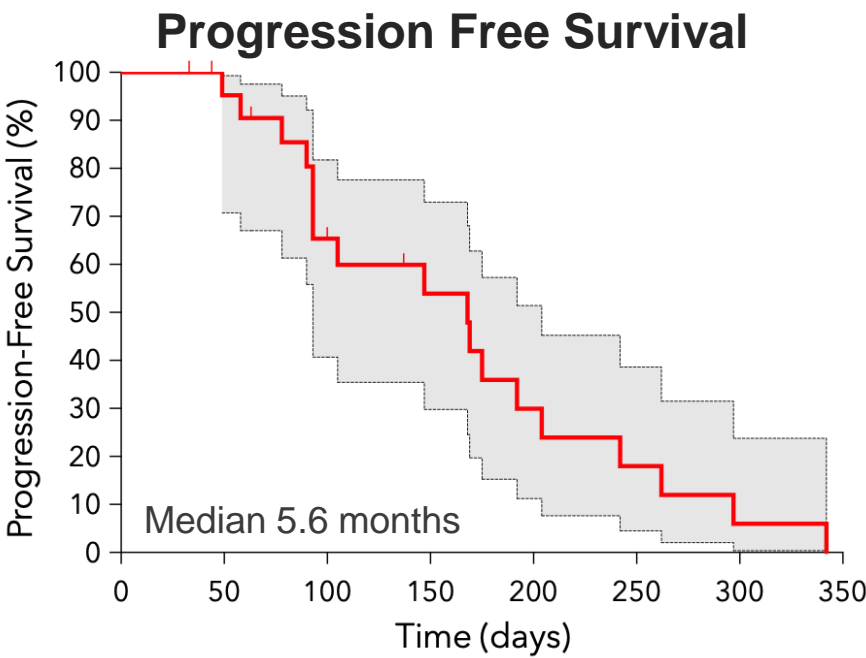
✚ Off Active FU (Unconfirmed PD)  
(e.g. Clinical prog/inv. decision)

➡ Alive (ongoing) □ Deceased



# Survival in Mesothelioma

ORR 21%, PFS 5.6 Months, OS 11.2 Months



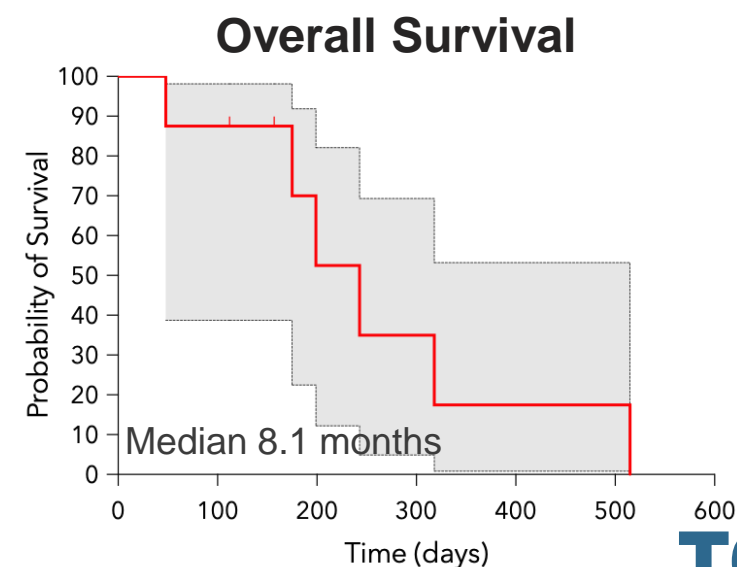
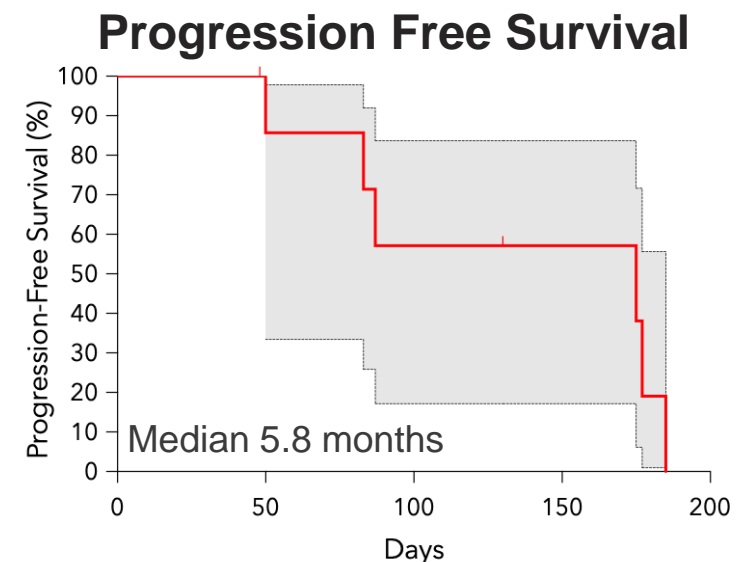
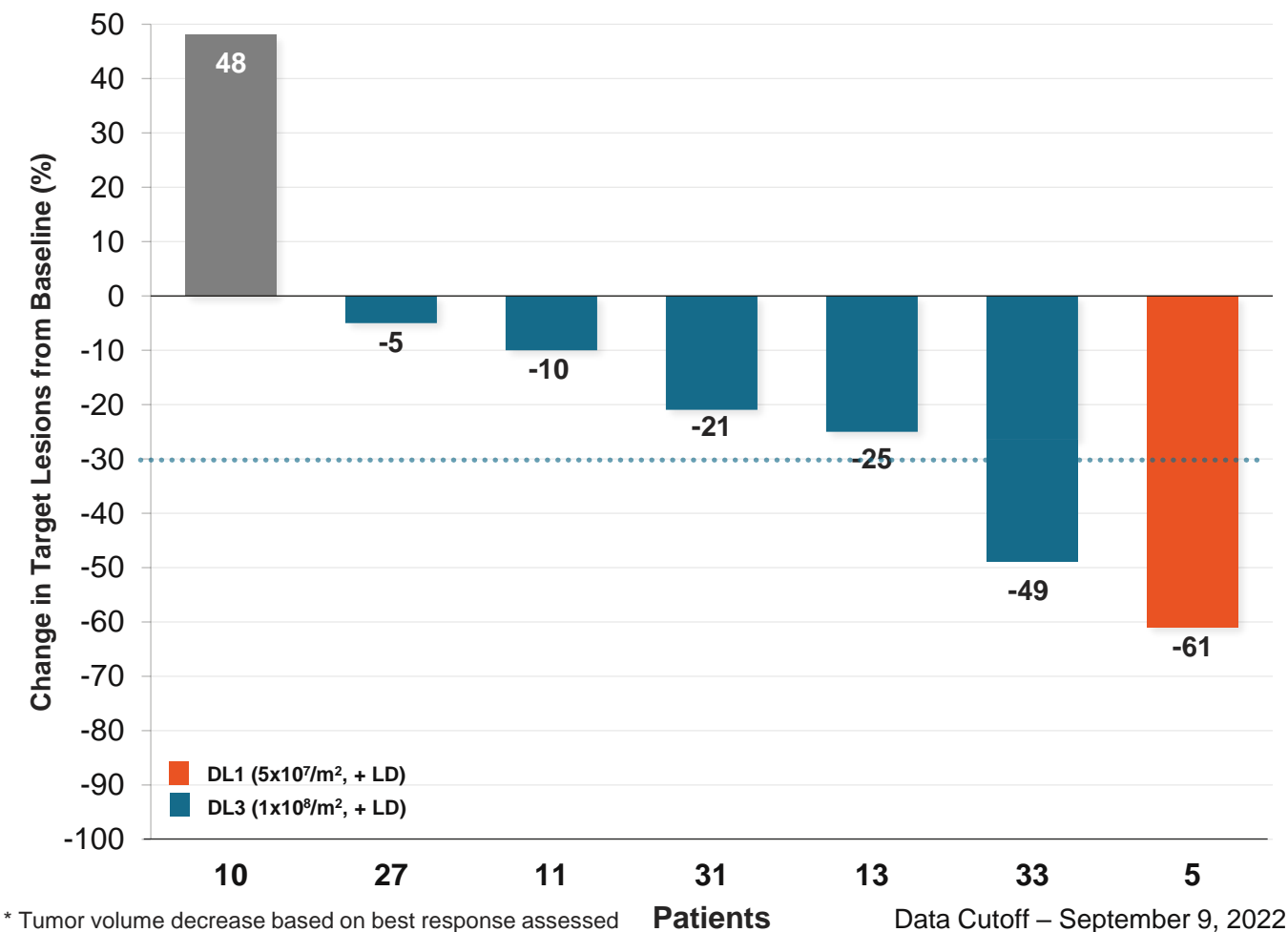
Study	n	ORR (%)	PFS (mo)	OS (mo)
Vinorelbine vs Supportive Care <sup>1</sup>	98	3.1	4.2	9.3
	56	1.8	2.8	9.1
Pembrolizumab vs Vinorelbine or Gemcitabine <sup>2</sup>	73	22	2.5	10.7
	71	6	3.4	12.4
Nivolumab vs Placebo <sup>3</sup>	221	11	3	10.2
	111	1	1.8	6.9

## Benchmarks in Second Line Post Platinum-Based Therapy

- 1. Fennell et al Phase 2 VIM Study. ASCO 2021
- 2. Popat et al Phase 3 PROMISE-meso Study. Ann Oncol 2020
- 3. Fennell et al Phase 3 CONFIRM Study. Lancet Oncol 2021

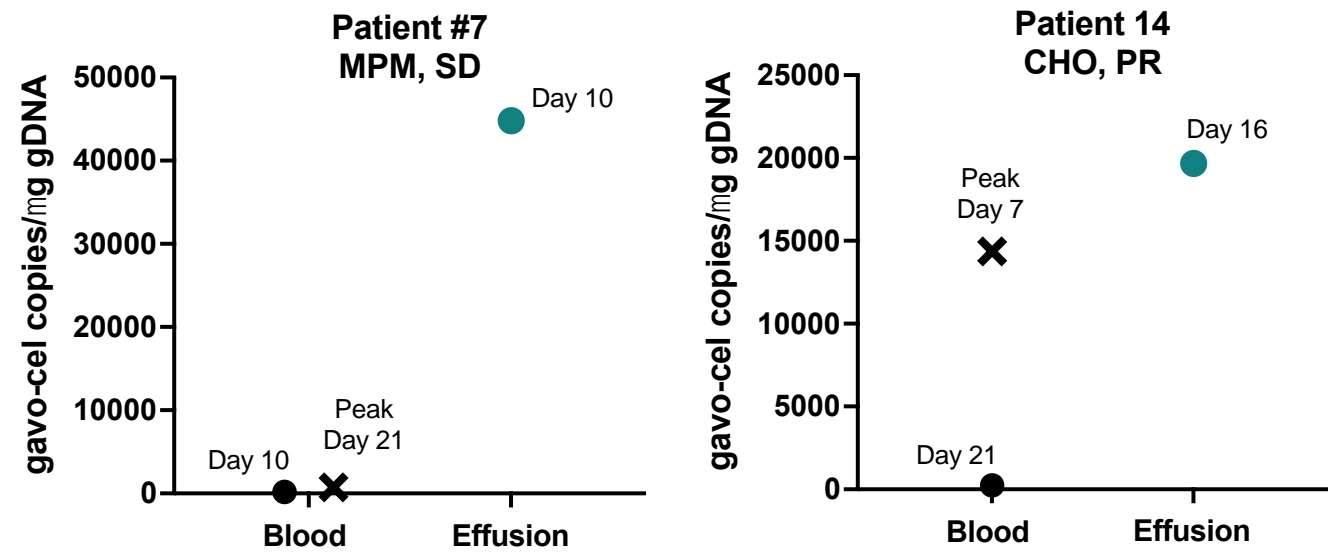
# Survival in Ovarian Cancer after gavo-cel Infusion

ORR 29%, PFS 5.8 Months, OS 8.1 Months

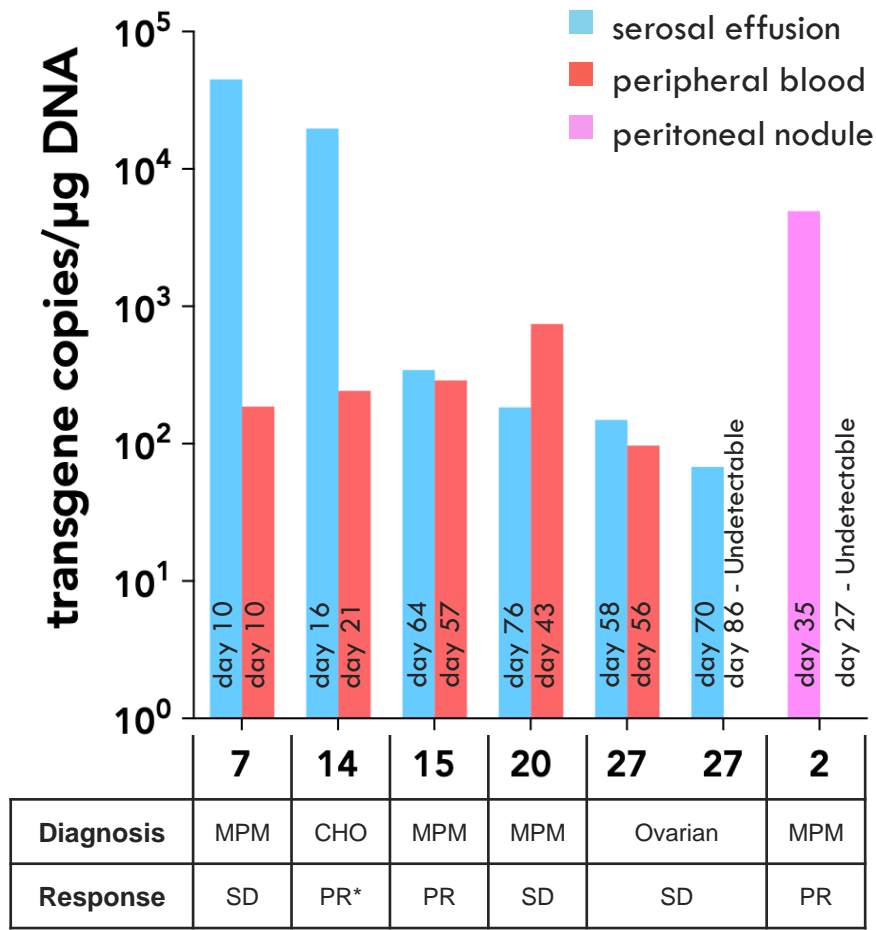


# Intratumor Infiltration and Persistence Greater Than in Blood

TRuC-T Cell Migration and Infiltration Evident from Serous Effusions



Analysis performed in a subset of patients (n=6); all analyzable samples showed detectable levels of gavo-cel, but not all showed increased expansion at disease sites

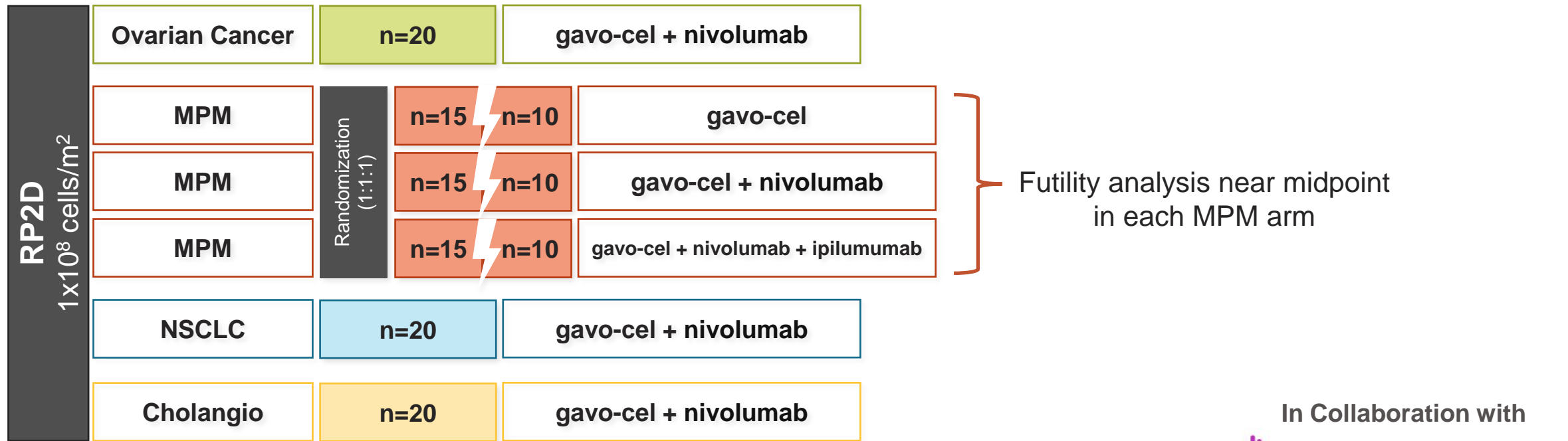


Data Cutoff – September 9, 2022

\* PR by Investigator Assessment

# Phase 2 Expansion Cohorts in MSLN+ Solid Tumors

PATIENT POPULATION: ≤5 PRIOR LINES OF THERAPY



## Key Objectives

- Primary: ORR (RECIST v1.1), DCR (ORR+SD)
- Secondary: PFS, OS

## Mesothelin Expression

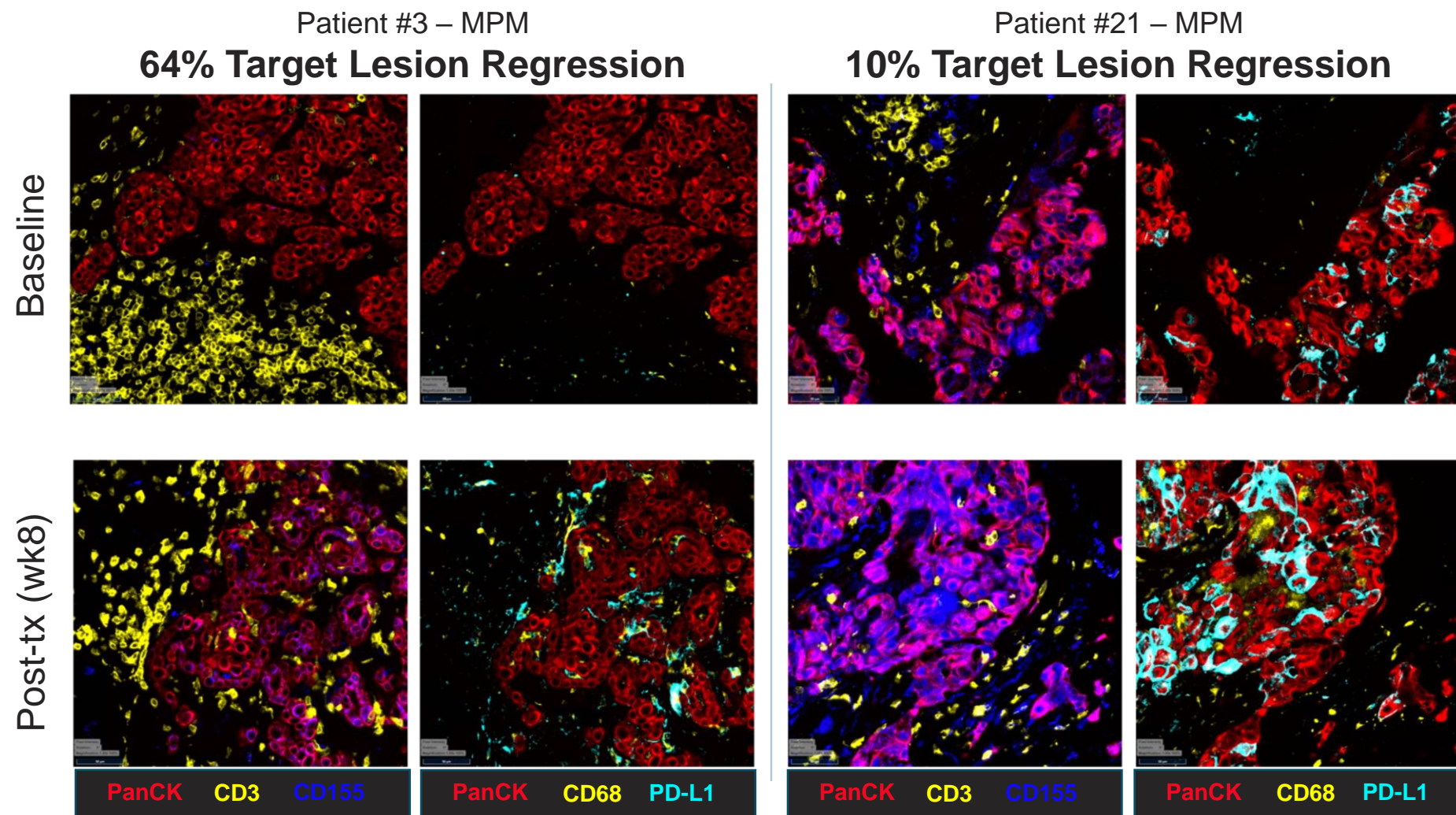
- MPM, Ovarian: ≥50%, 2+/3+
- NSCLC, Cholangio: ≥50%, 1+/2+/3+

## Retreatment

- Patient with a confirmed response (i.e. PR or CR) and then exhibits symptoms or signs of PD
- Patients with SD for at least 8 weeks

# CPIs Expected to Improve Activity of TRuC-T Cells

*Immunoinhibitory Mechanisms May Play A Role in Resistance*



PanCK = tumor marker; CD3 = T cell marker; CD68 = TAM marker; CD155 = TIGIT ligand; PD-L1 = PD-1 ligand  
Multiparameter immunofluorescence assay performed using MultiOmx™ (Neogenomics)





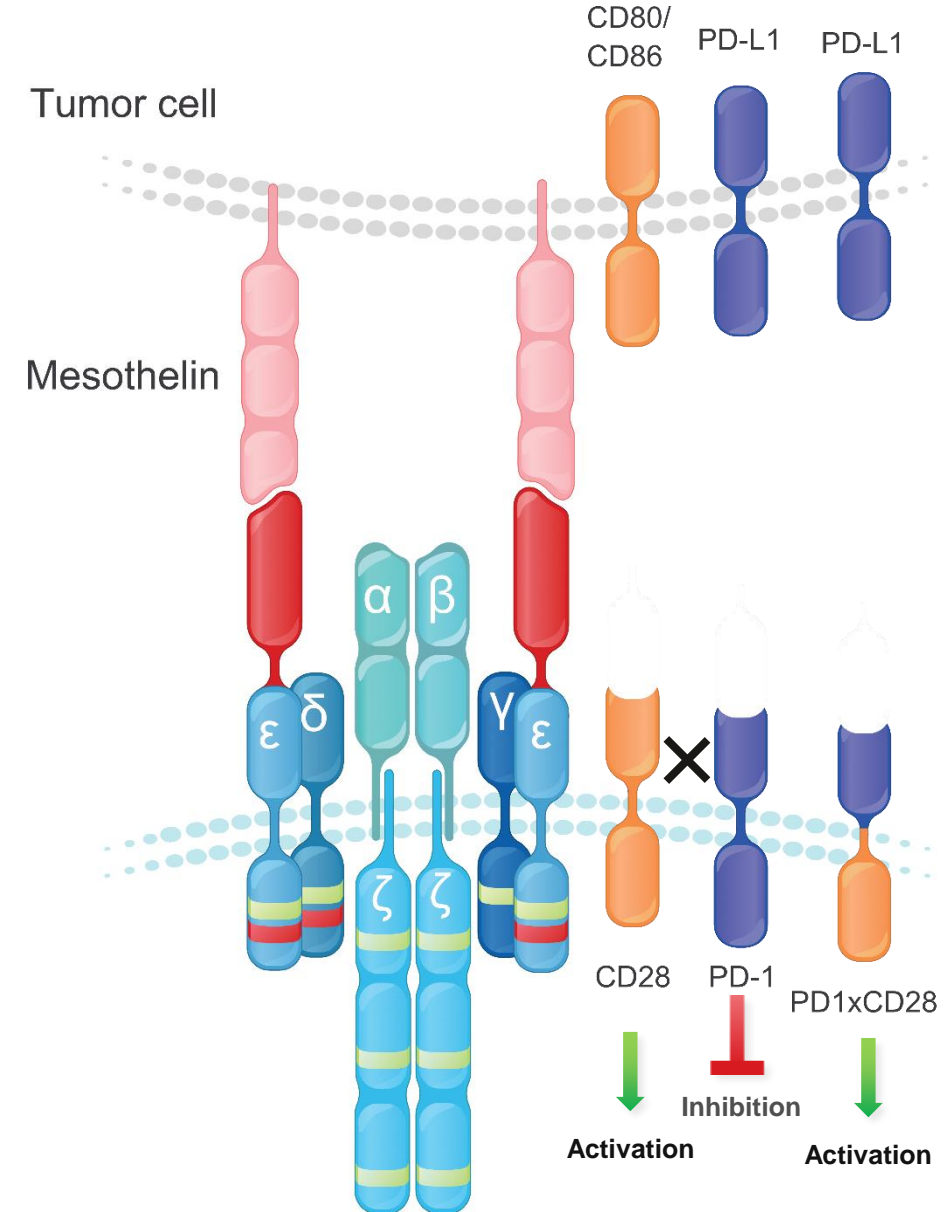
# Expanding the Base

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*Innovating the Next Generation of TRuCs*

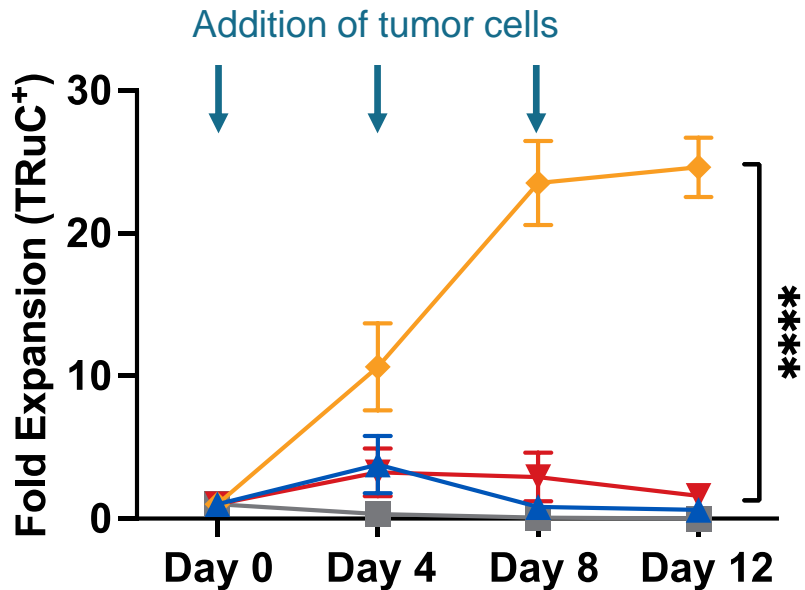
# Enhancing gavo-cel with a PD-1:CD28 Switch Receptor

- PD-1:CD28 switch designed to convert PD-L1/L2 inhibitory function into a potent costimulatory signal
- Costimulation occurs only in a PD-L1/2 rich tumor microenvironment upon TRuC and PD-1 ligation resulting in a more targeted signal enhancement
- Mesothelin-targeting TRuCs that co-express a PD-1:CD28 switch in vivo featured:
  - Enhanced early TCR downstream signaling
  - Significantly increased proliferation
  - Prevented exhaustion upon repeated antigen stimulation
  - Enhances efficacy of gavo-cel against PD-L1 overexpressing tumors

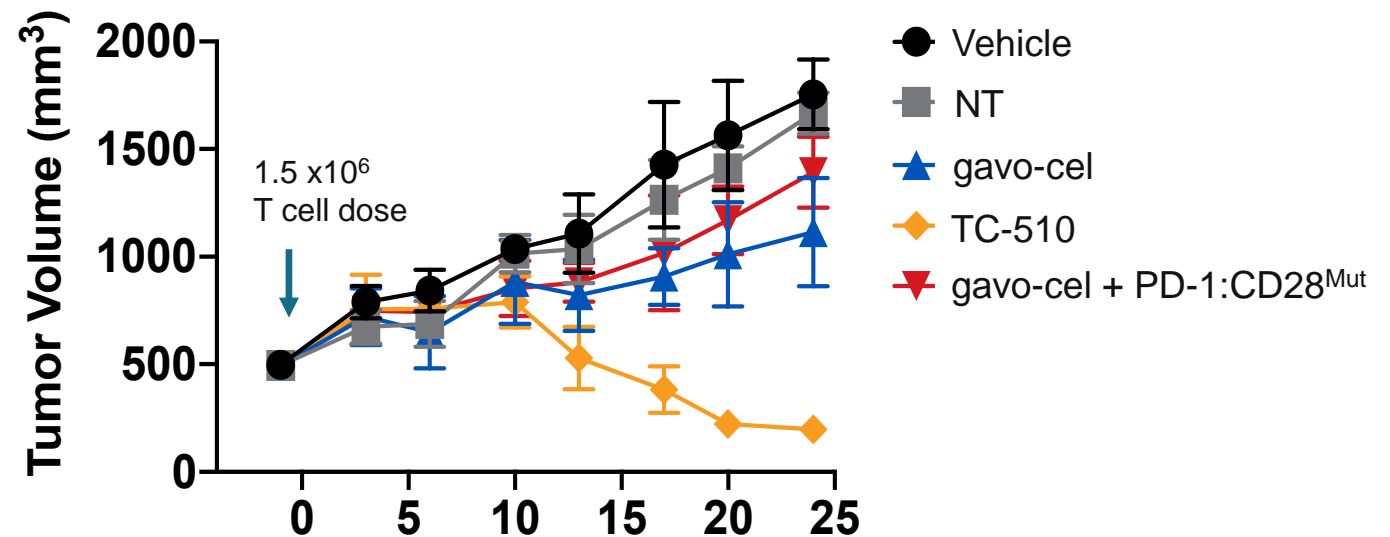


# Against Tumors with High PD-L1 Expression, TC-510 Shows Enhanced Proliferation and Superior Efficacy

## Expansion upon Repeated Stimulation



## Anti-Tumor Activity in Mouse Model

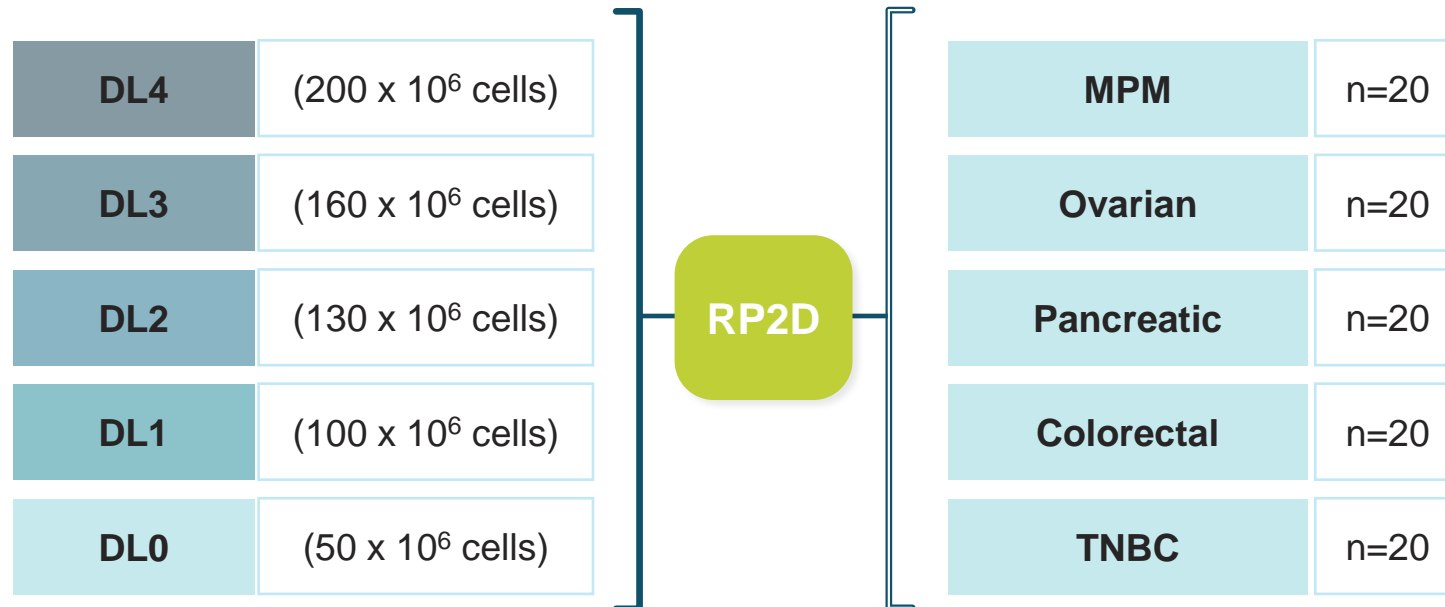
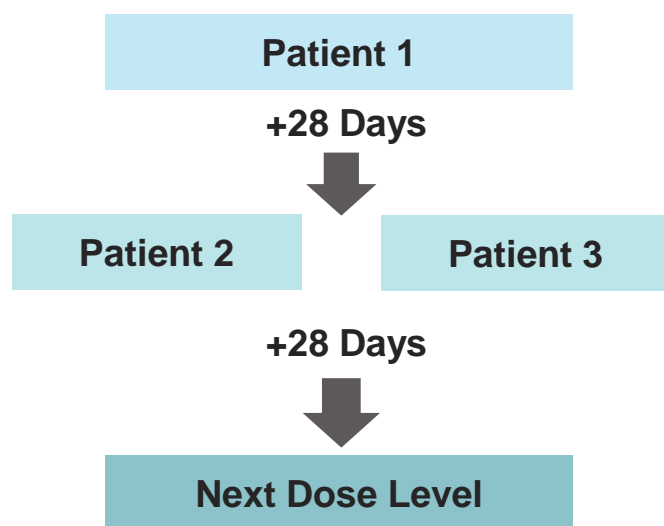


MSTO-M/PDL1 model expressing high MSLN and PD-L1

# TC-510 Phase 1 Trial in MSLN+ Solid Tumors

PATIENT POPULATION: ≤5 PRIOR LINES OF THERAPY

Each dosing cohort consists of:



## Key Objectives

- Primary: Safety, establish RP2D
- Secondary: ORR (RECIST v1.1), DoR, DCR (ORR+SD), PFS, OS

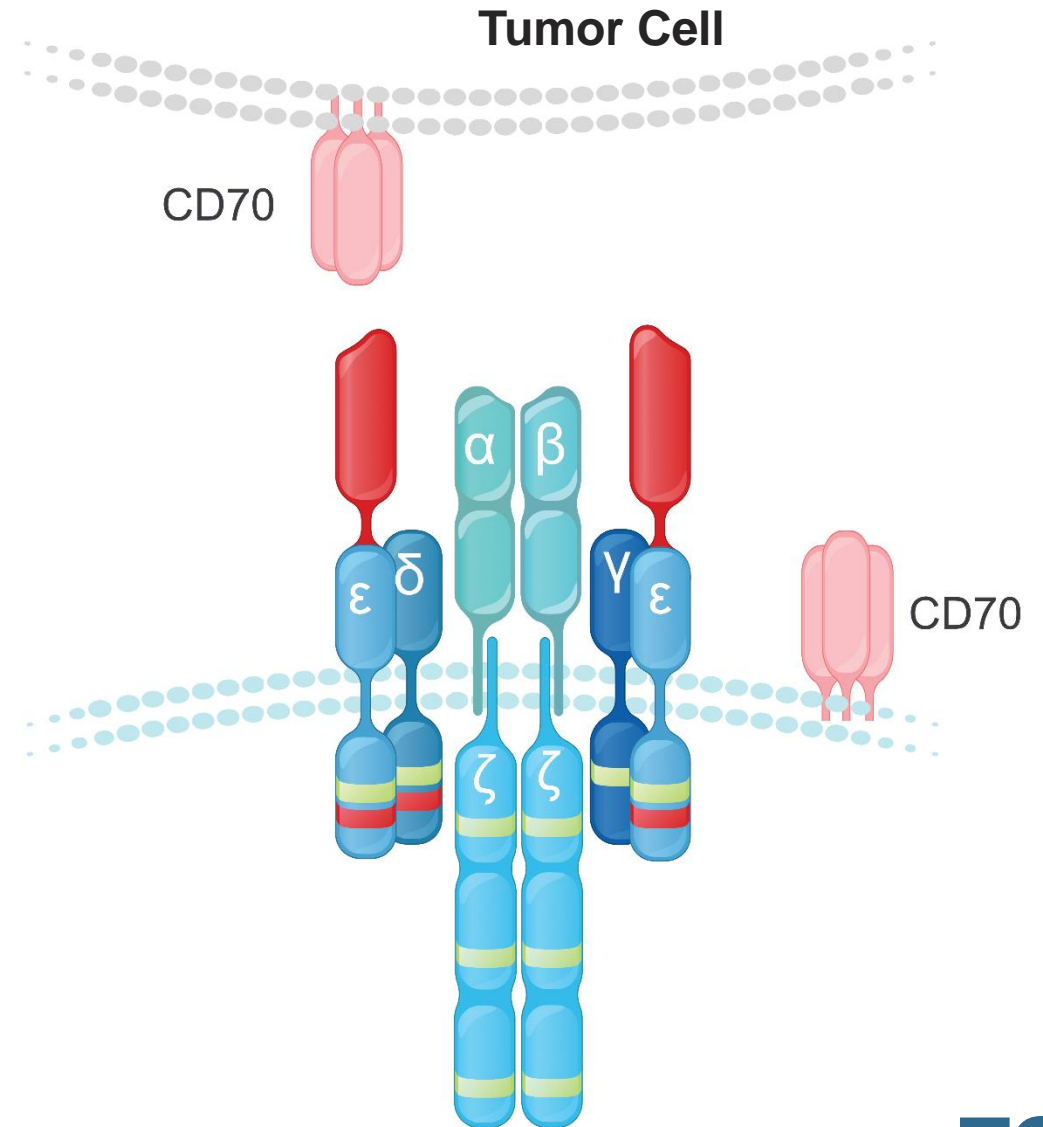
## Mesothelin Expression

- ≥50% 1+/2+/3+

# CD70: Highly Attractive Target with an Innate Fratricide Challenge

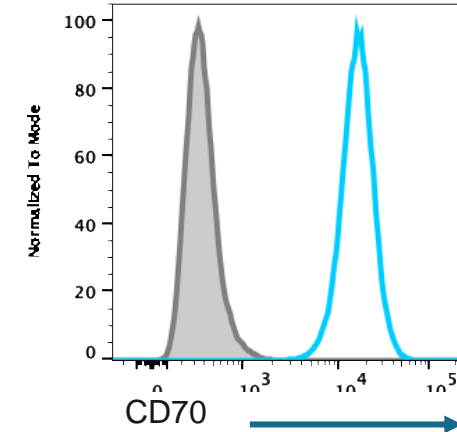
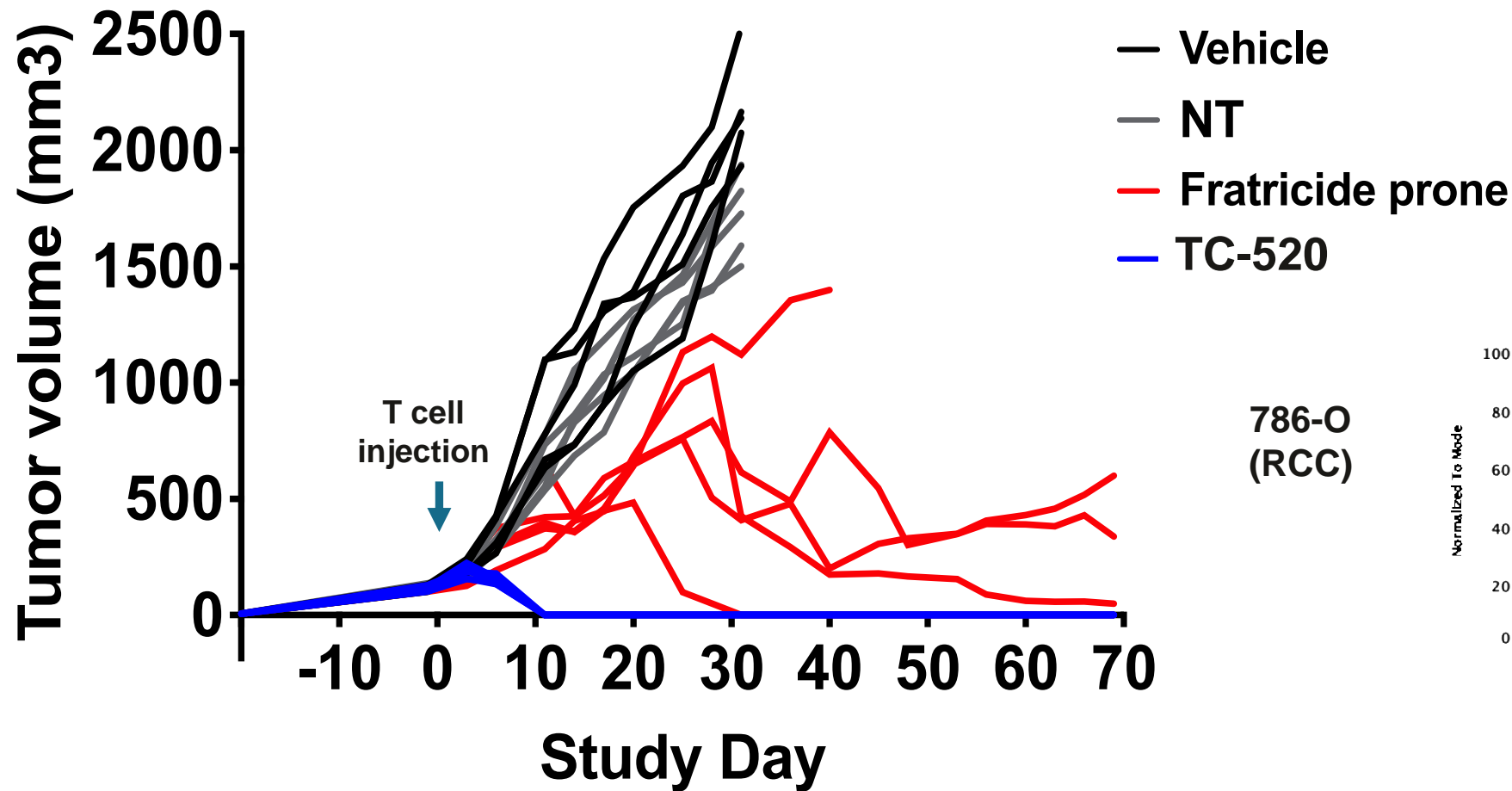
*Up to 141,000 Patients Expressing CD70 in the US*

- Versatile tumor target: expressed in hematological malignancies (AML, lymphoma) and solid tumors (RCC, NSCLC, OC)
  - Expression in normal cells limited to a subset of activated T cells, B cells, and dendritic cells
  - Expression in activated T cells renders CD70-directed T cell therapies susceptible to fratricide
- Clinically validated: POC demonstrated in AML with αCD70 mAb in AML (argenx)
- Path to first-in-class autologous CD70 cell therapy
  - Most advanced CAR-T programs by Allogene and CRISPR are allogeneic targeting RCC

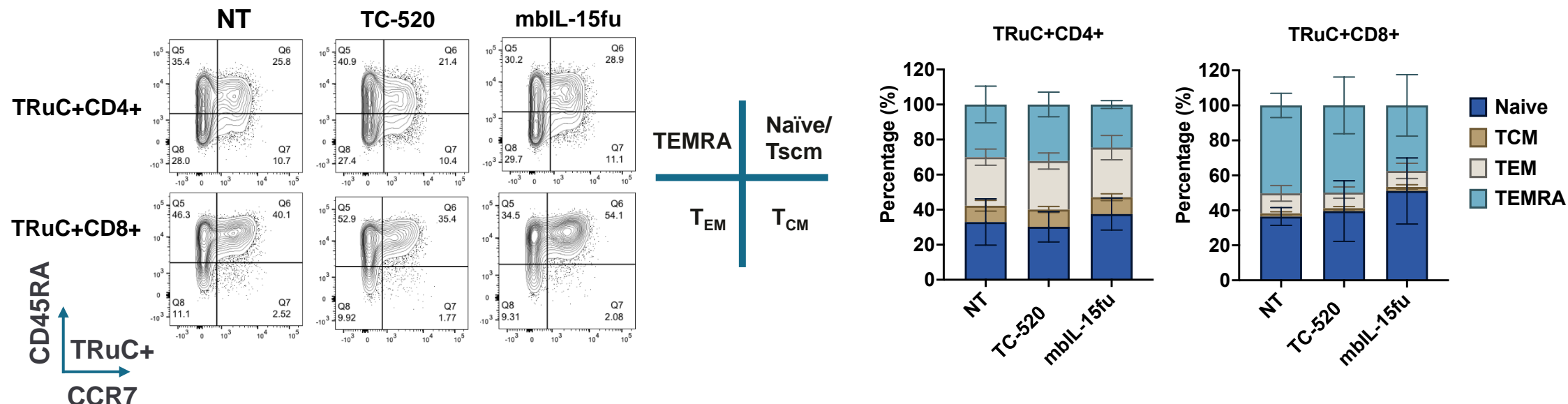




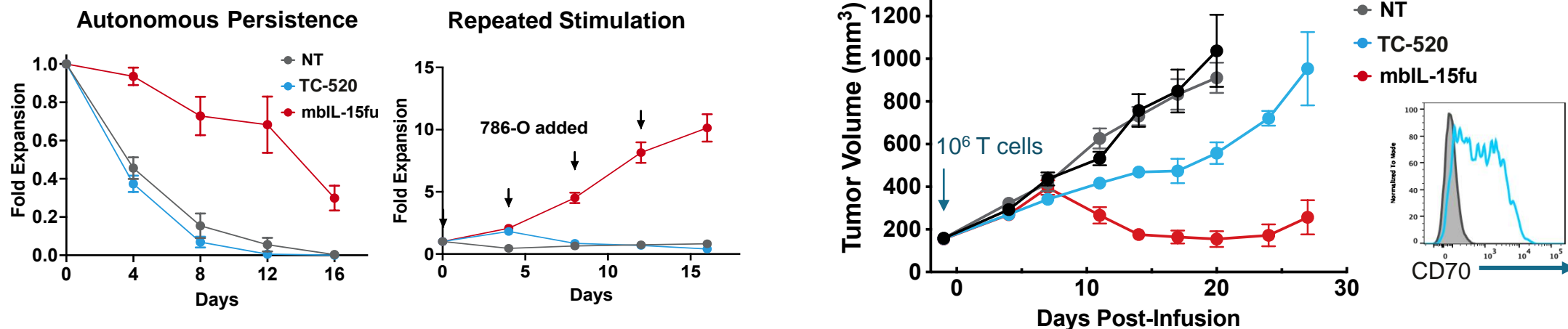
# TC-520 Exhibits Potent and Persistent *In Vivo* Efficacy



# IL-15 Enhancement Improves TC-520 Phenotype and Function



## In Vivo Efficacy at Suboptimal Dose in CD70 low H1975 NSCLC model





An elderly couple is walking on a grassy hill, looking out over a vast landscape. The woman is wearing a beige jacket and a bright yellow scarf, and the man is wearing a brown jacket and a grey scarf. They are holding hands and looking towards the right. The background shows a dense forest of trees with autumn foliage, and mountains are visible in the distance under a hazy sky.

# THE POWER OF tomorrow

Engaging the TCR to Transform  
the Treatment of Solid Tumors

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Thank You

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