
THE POWER OF tomorrow
Engaging the TCR to Transform
the Treatment of Solid Tumors
Corporate Presentation
September 2022
TCR2
THERAPEUTICS

Forward Looking Statements

This presentation has been prepared by TCR2 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 June 30, 2022, as filed with the SEC on August 8, 2022, and in our future filings with the SEC available at the SEC's website at 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.

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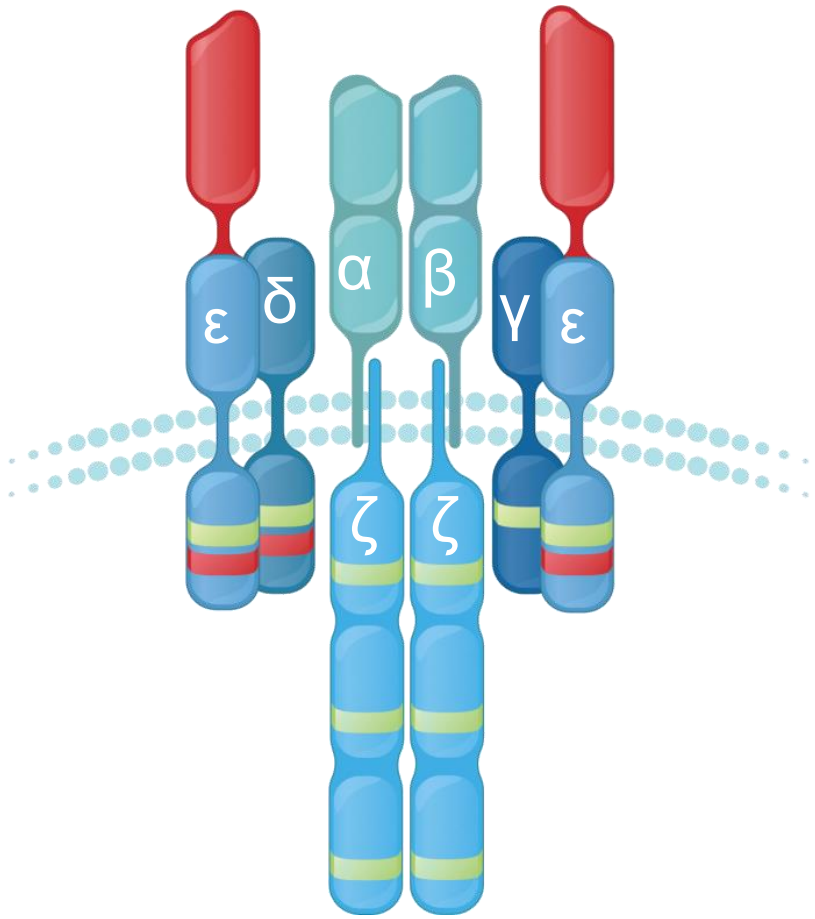
Innovating the Natural Power of the TCR for Solid Tumors



TRuC® Platform
(**T** Cell **R**eceptor F**u**sion **C**onstruct)

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

TCR, T Cell Receptor; HLA, Human Leukocyte Antigen

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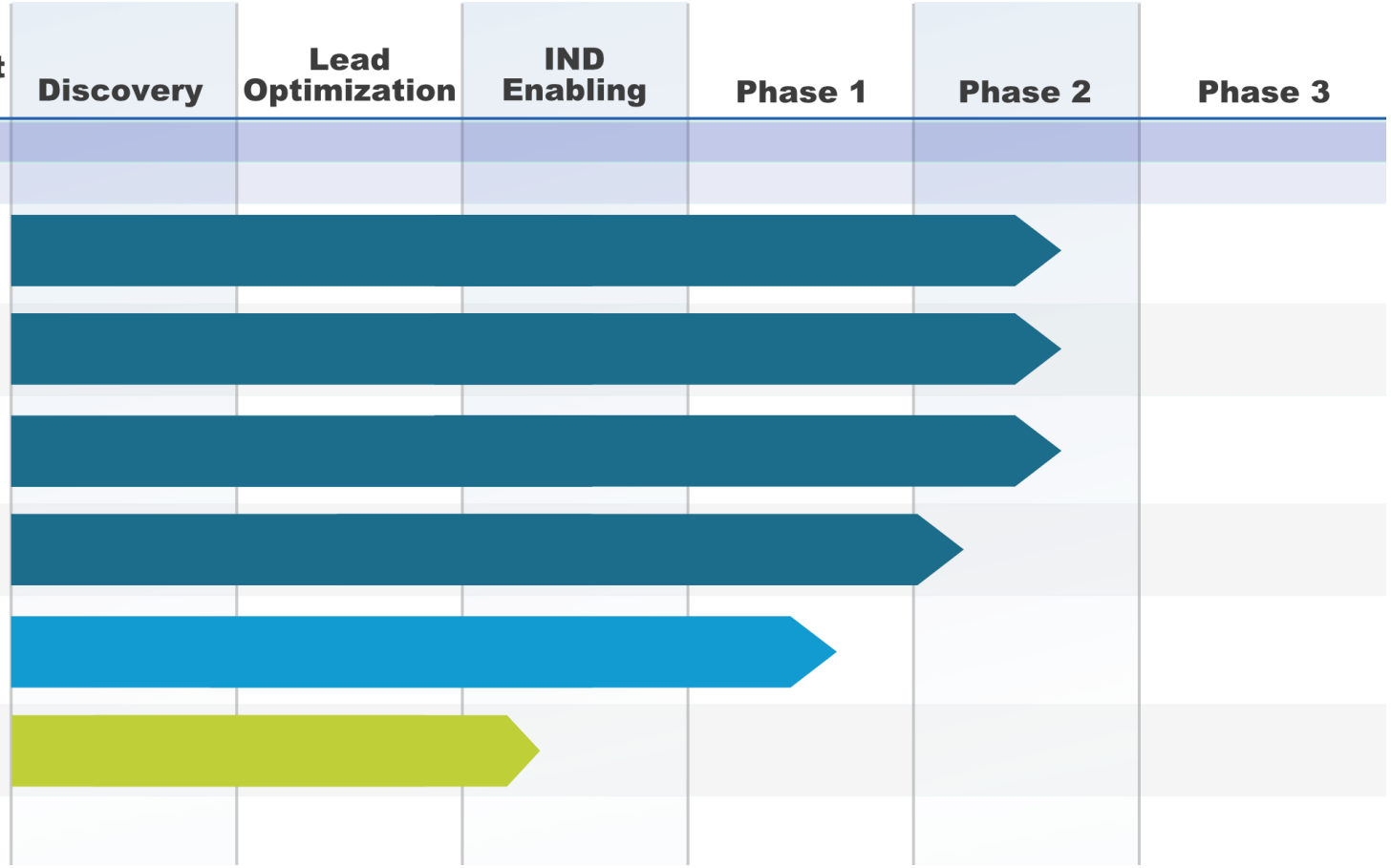
Refocused Pipeline to Deliver Near-Term Clinical Data

Program	Indication(s)	Target	Enhancement / Combo
Oncology			
gavo-cel	Ovarian cancer (Treating)	MSLN	Checkpoint inhibitor
gavo-cel	MPM (Treating)	MSLN	Checkpoint inhibitor
gavo-cel	NSCLC (Enrolling)	MSLN	Checkpoint inhibitor
gavo-cel	Cholangiocarcinoma (Next wave)	MSLN	Checkpoint inhibitor
TC-510	Ovarian cancer, MPM,Pancreatic, Colorectal, TNBC	MSLN	PD-1 switch
TC-520	RCC, AML	CD70	IL-15



MSLN, Mesothelin; MPM, Malignant Pleural/Peritoneal Mesothelioma; NSCLC, Non-Small Cell Lung Cancer; TNBC, Triple Negative Breast Cancer; RCC, Renal Cell Carcinoma; AML, Acute Myeloid Leukemia

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Leading the Way with gavo-cel

Stage of Development: Phase 2

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Significant Potential Opportunity in Mesothelin-Expressing Solid Tumors

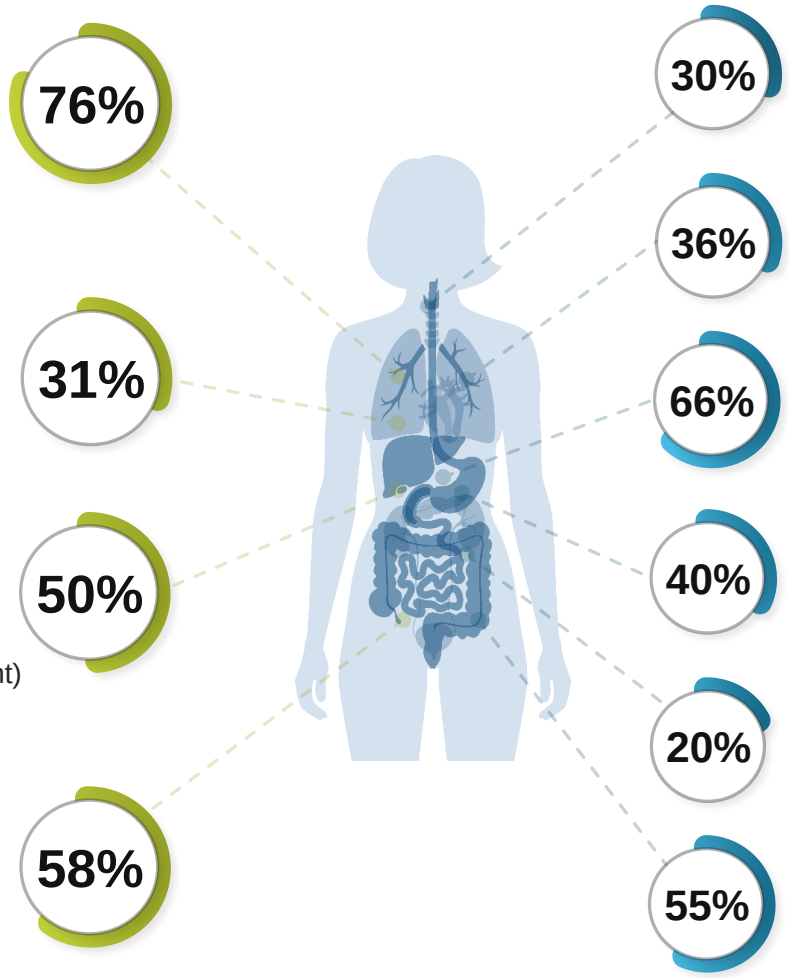
~215,000 Patients Across Multiple Target Indications

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, Tozbikian 2014

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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 ≥ 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

DCR, Disease Control Rate; ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival; RP2D, Recommended Phase 2 Dose; AE, Adverse Event; CRS, Cytokine Release Syndrome; MPM, Malignant Pleural/Peritoneal Mesothelioma; CPI, Checkpoint Inhibitor; NSCLC, Non-Small Cell Lung Cancer; MSLN, Mesothelin

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Grade ≥3 Treatment Emergent Adverse Events

Adverse Event	DL 0 (no LD) $5x10^7/m^2$ n=1 (%)	DL 1 $5x10^7/m^2$ n=8 (%)	DL 2 (no LD) $1x10^8/m^2$ n=1 (%)	RP2D DL 3 $1x10^8/m^2$ n=13 (%)	DL 3.5 $3x10^8/m^2$ n=5	DL 4 (no LD) $5x10^8/m^2$ n=1 (%)	DL 5 $5x10^8/m^2$ n=3 (%)	Overall n=32 (%)
Hematologic								
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)
On Target / On Tumor								
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
On Target / Off Tumor								
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)
Other								
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

DL, Dose Level; LD, Lymphodepletion; RP2D, Recommended Phase 2 Dose; HLH, Hemophagocytic Lymphohistiocytosis; MAS, Macrophage Activation Syndrome

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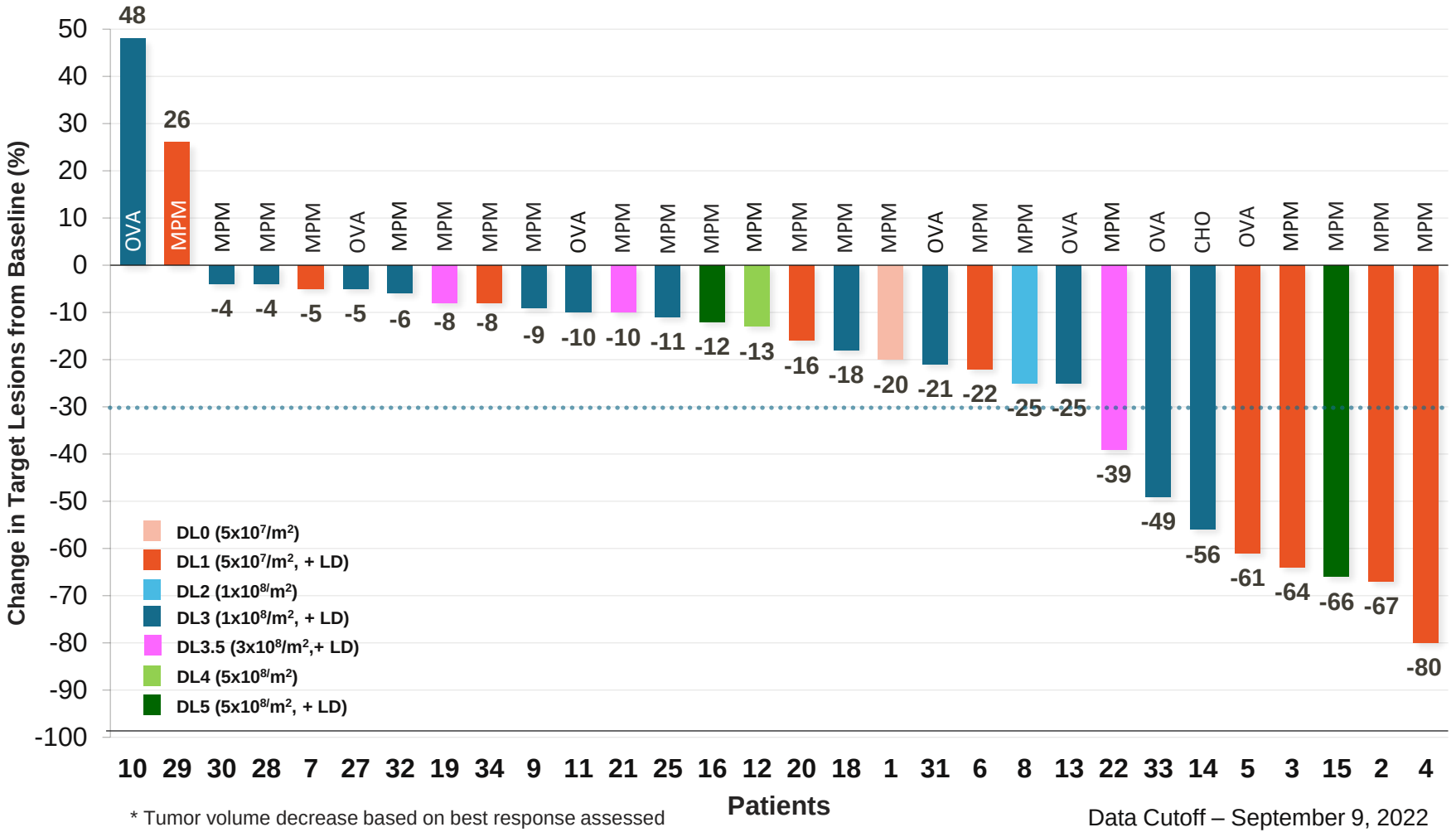
Consistent Tumor Regression in Patients with gavo-cel

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



* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022

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

DL, Dose Level; LD, Lymphodepletion; DCR, Disease Control Rate; ORR, Overall Response Rate; PR, Partial Response; SD, Stable Disease

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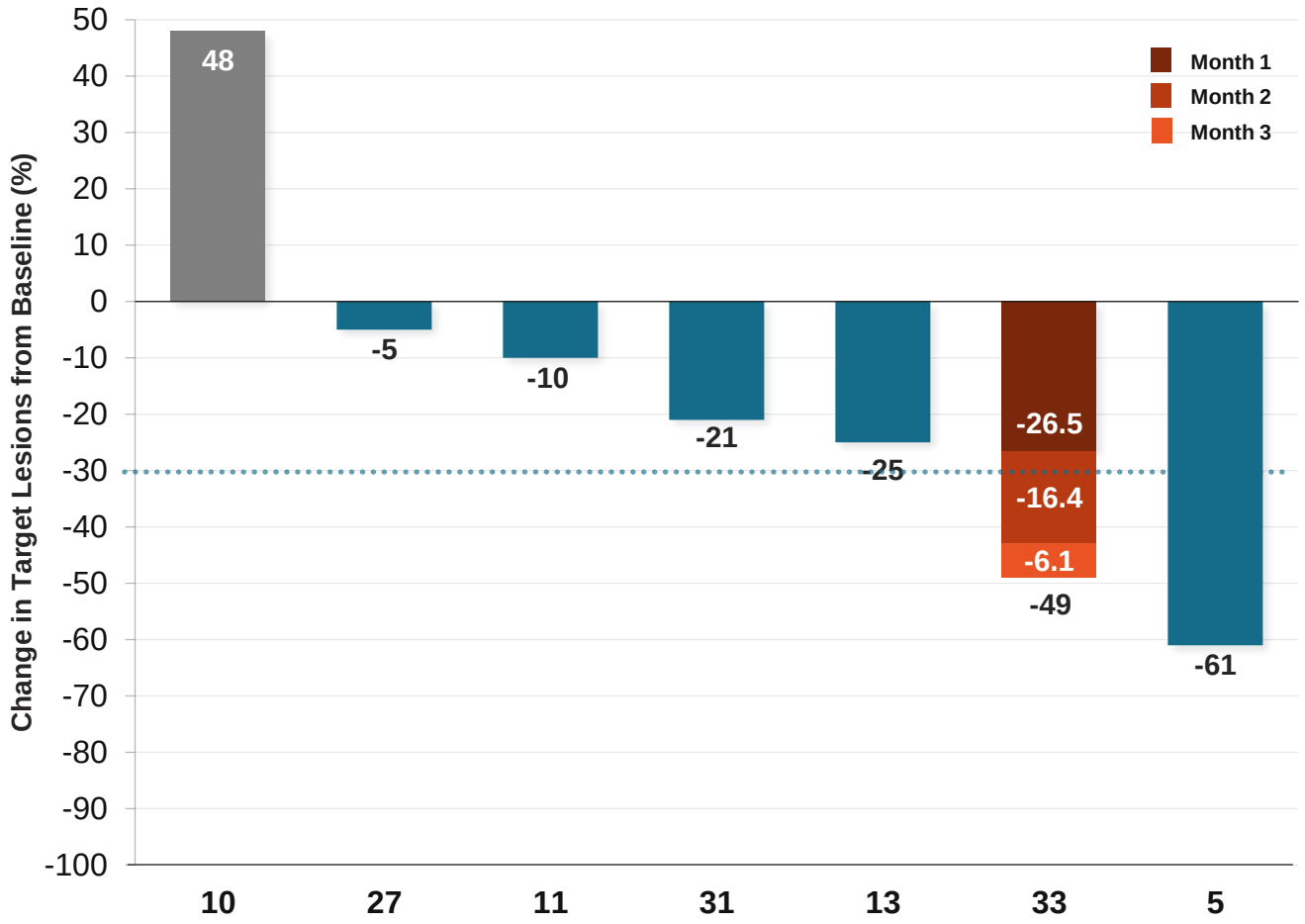
Promising Signal in Platinum Refractory Ovarian Cancer

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



* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022

ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival; LD, Lymphodepletion

TCR2 THERAPEUTICS

Patient 33 – Platinum Refractory Ovarian Cancer

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

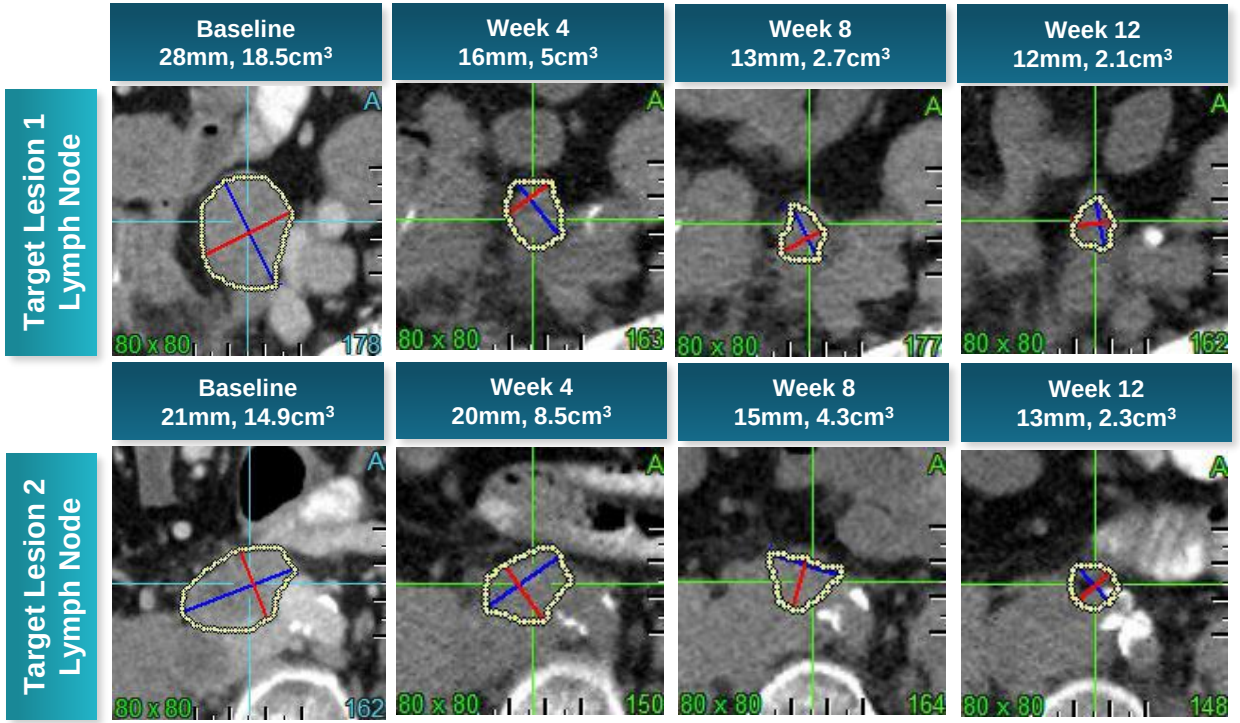
66-year-old female,

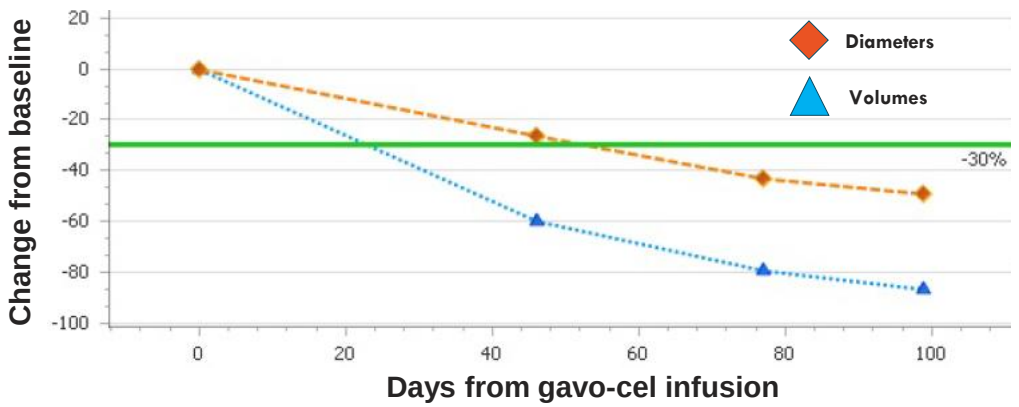
High grade, Stage IV serous ovarian cancer

- *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 $1x10^8/m^2$ (RP2D)





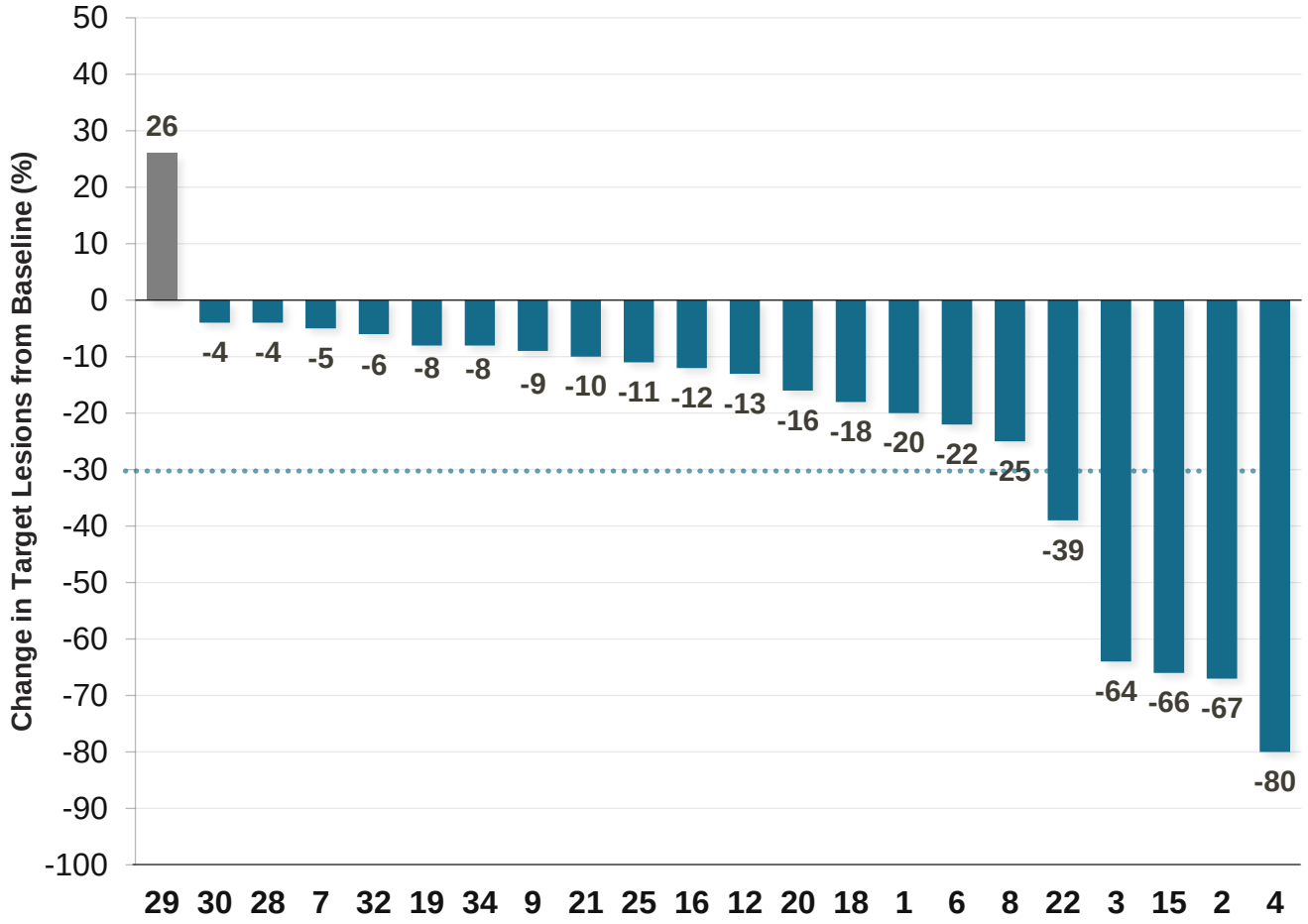
Phase 1 Data Support a Path Forward as Mesothelioma Leader

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



* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022

ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival; LD, Lymphodepletion

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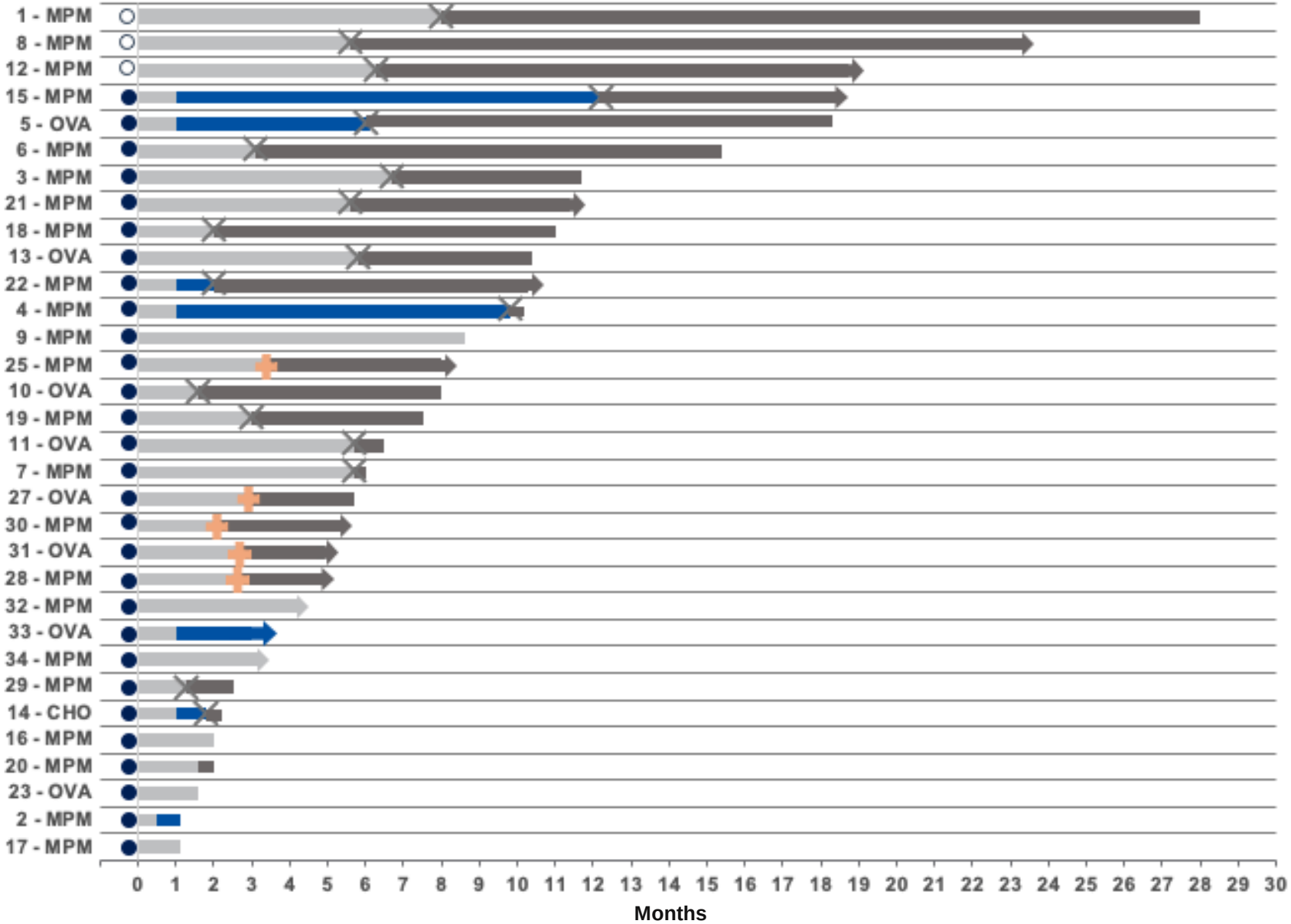
Patient Response and Follow-up as of September 9th, 2022



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**

CHO, Cholangiocarcinoma; SD, Stable Disease; PR, Partial Response; CR, Complete Response; PD, Progressive Disease; FU, Follow-Up

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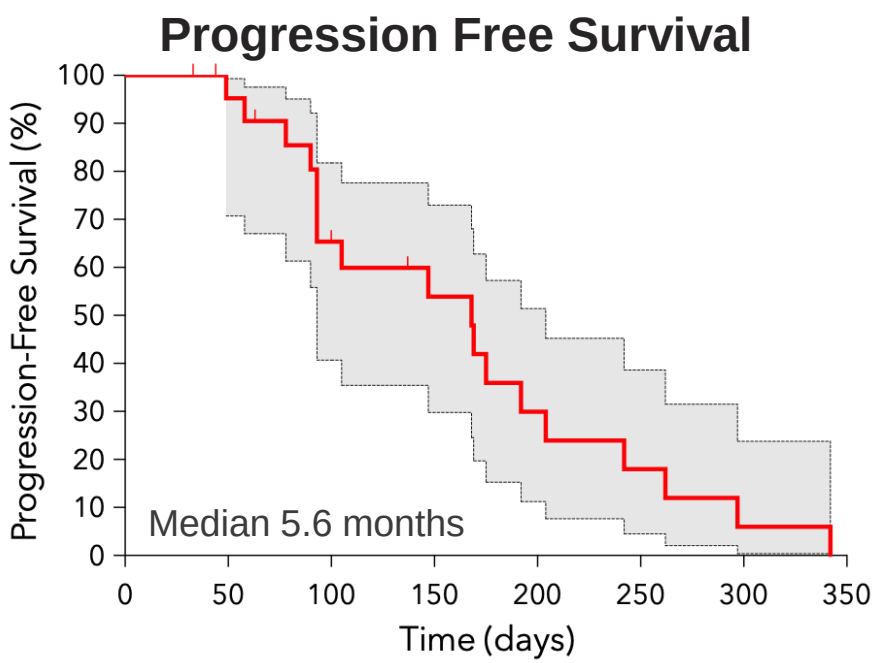
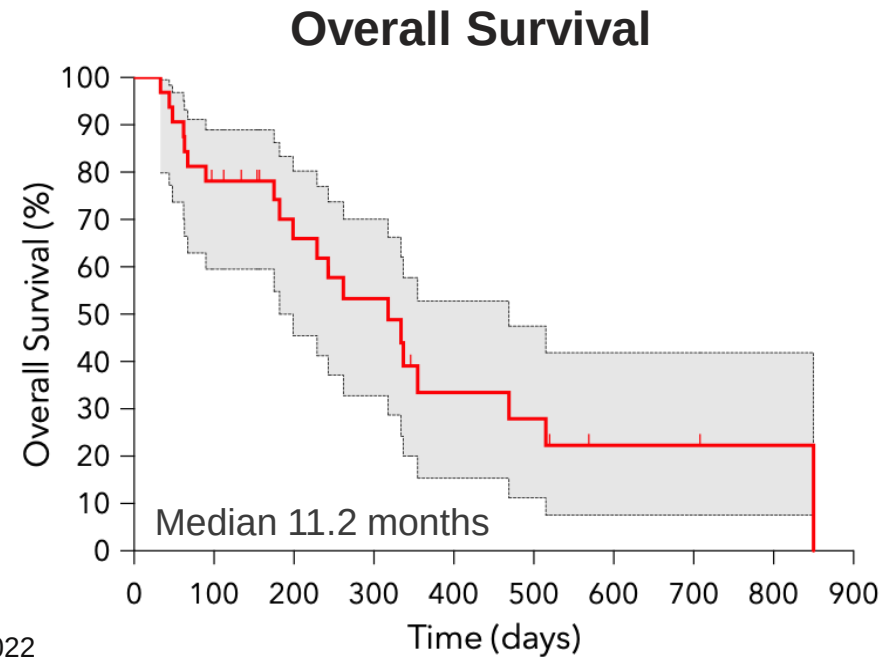
Survival in Mesothelioma

ORR 21%, PFS 5.6 Months, OS 11.2 Months





Data Cutoff – September 9, 2022

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

ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival

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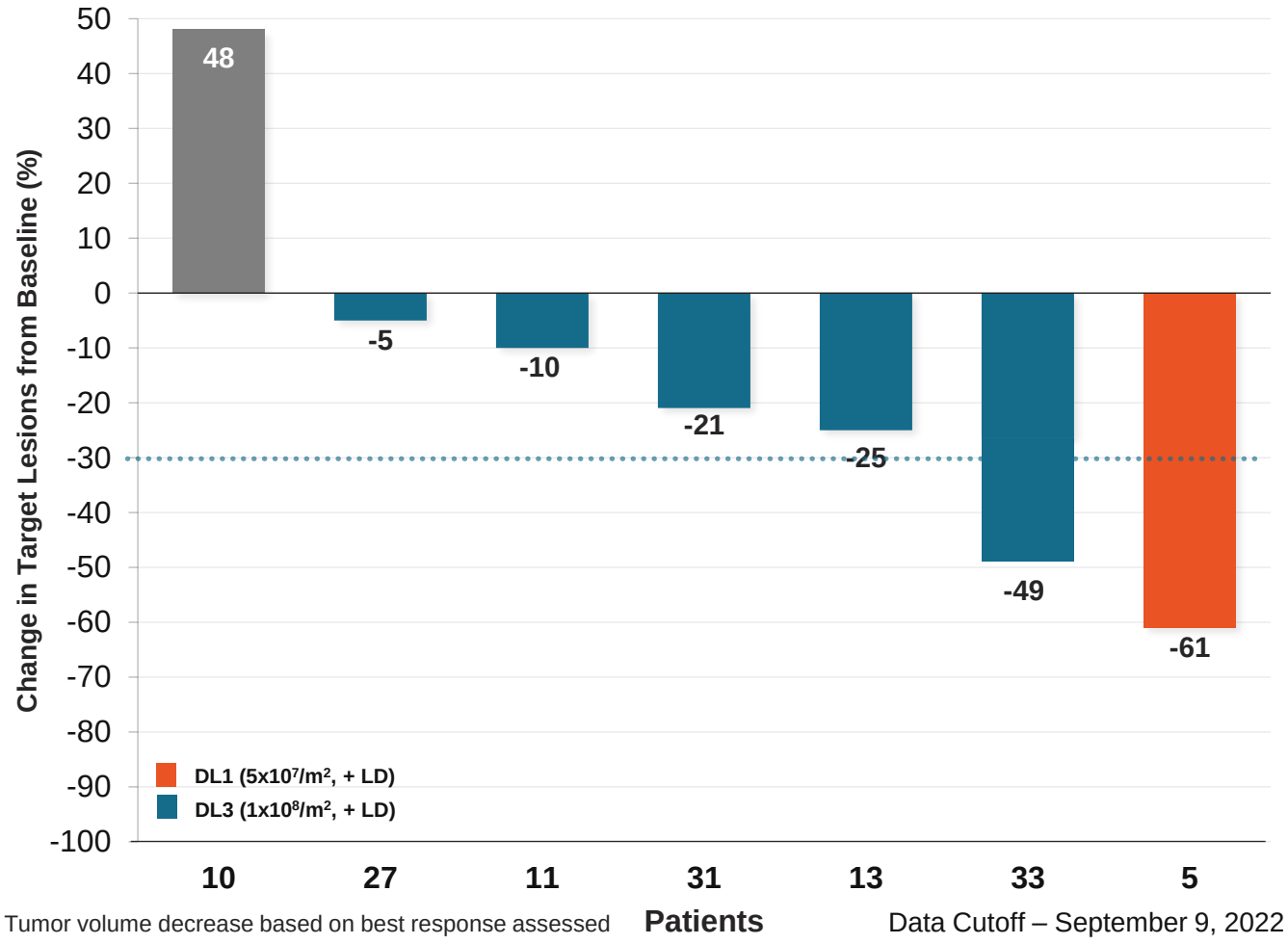
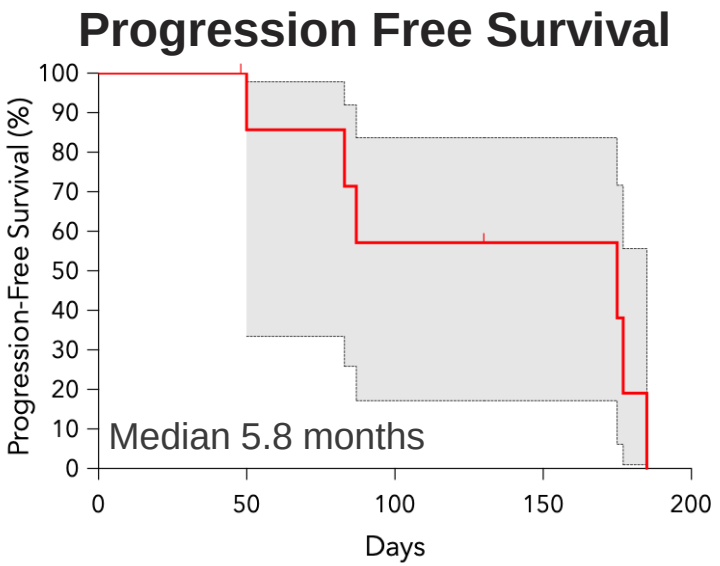
Survival in Ovarian Cancer after gavo-cel Infusion

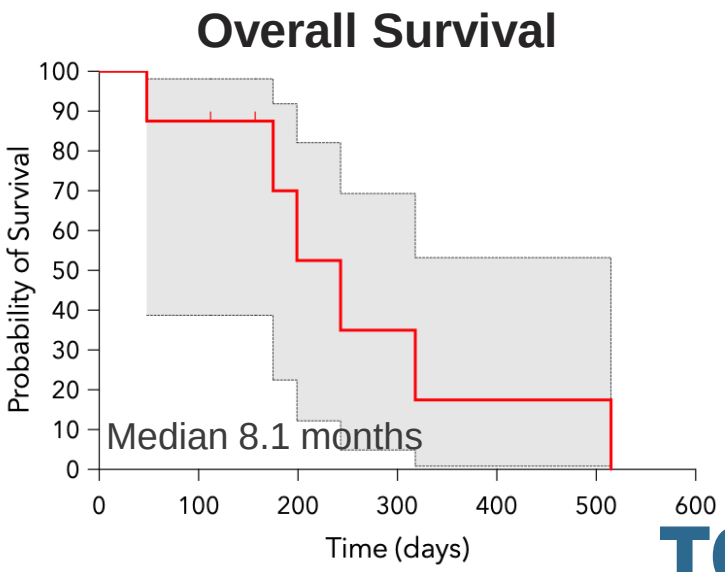
ORR 29%, PFS 5.8 Months, OS 8.1 Months



* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022

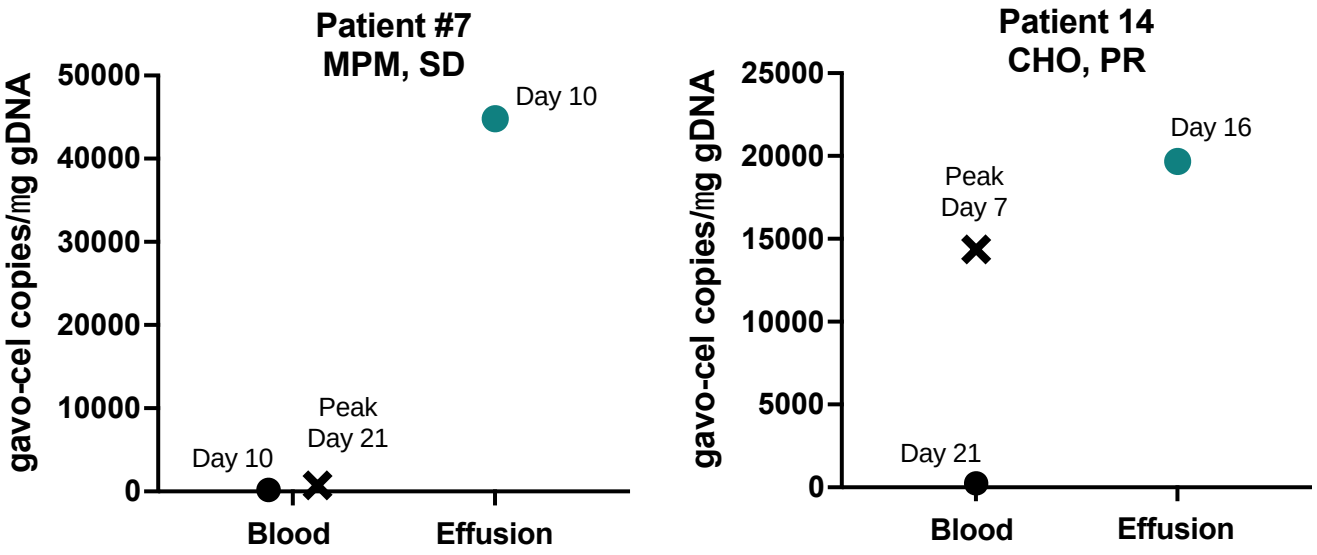




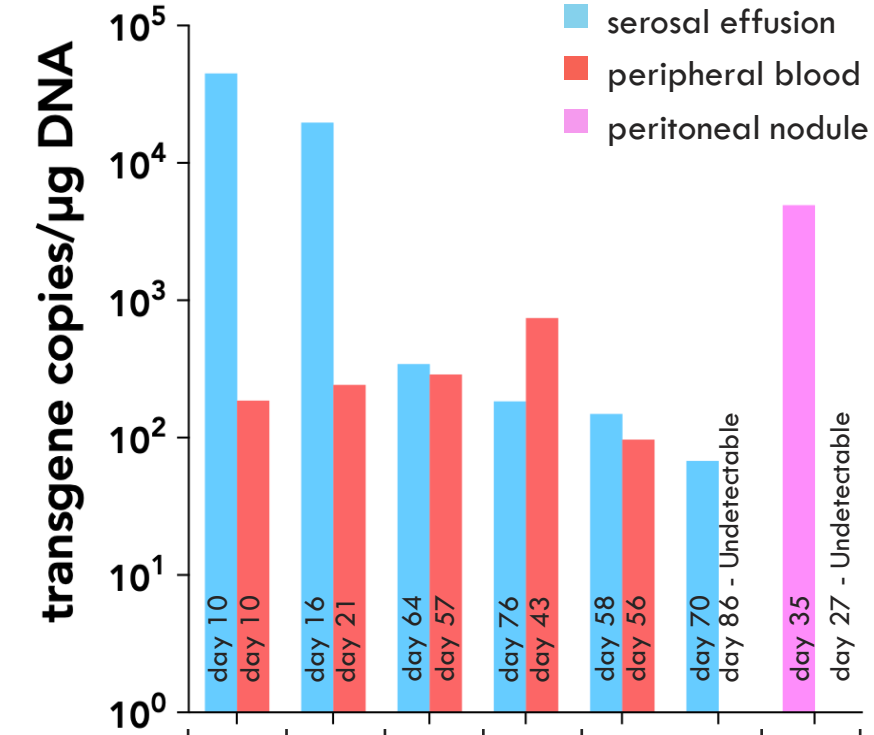
ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival; DL, Dose Level; LD, Lymphodepletion

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



	7	14	15	20	27	27	2
Diagnosis	MPM	CHO	MPM	MPM	Ovarian		MPM
Response	SD	PR*	PR	SD	SD		PR

Data Cutoff – September 9, 2022

* PR by Investigator Assessment

MPM: Malignant Pleural/Peritoneal Mesothelioma; CHO: Cholangiocarcinoma; PR: Partial Response; SD: Stable Disease

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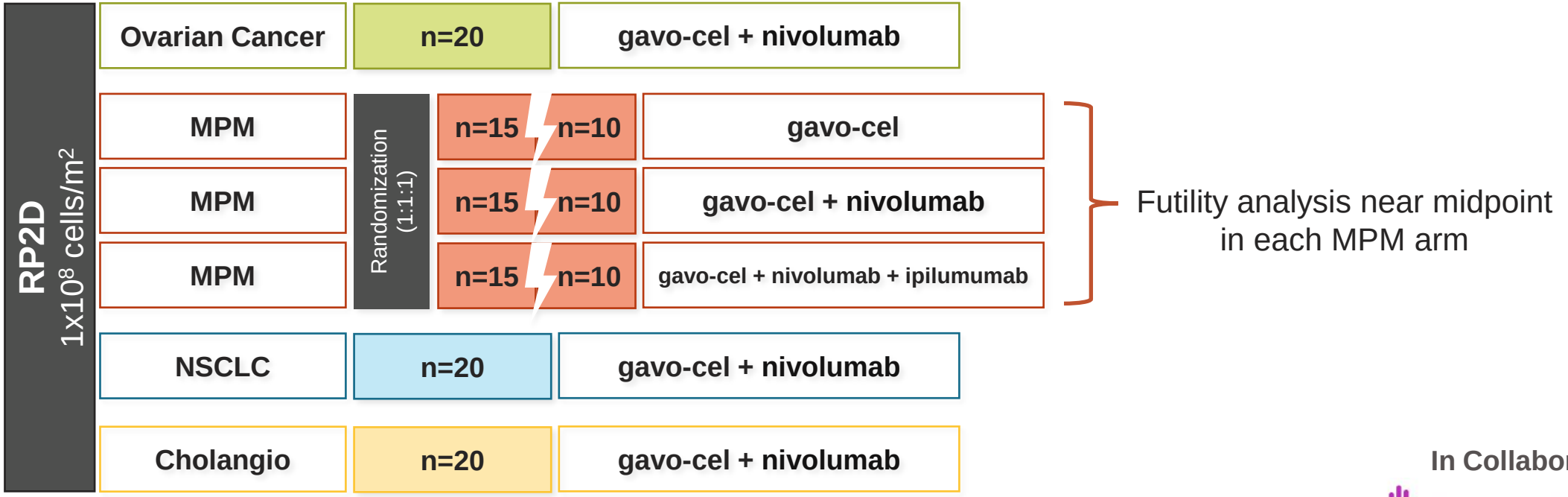
Phase 2 Expansion Cohorts in MSLN+ Solid Tumors

PATIENT POPULATION: ≤5 PRIOR LINES OF THERAPY



In Collaboration with Bristol Myers Squibb™

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

LD, Lymphodepletion; CPI, Checkpoint Inhibitor; RP2D, Recommended Phase 2 dose; MPM, Malignant Pleural/Peritoneal Mesothelioma; NSCLC, Non-Small Cell Lung Cancer; Cholangio, Cholangiocarcinoma

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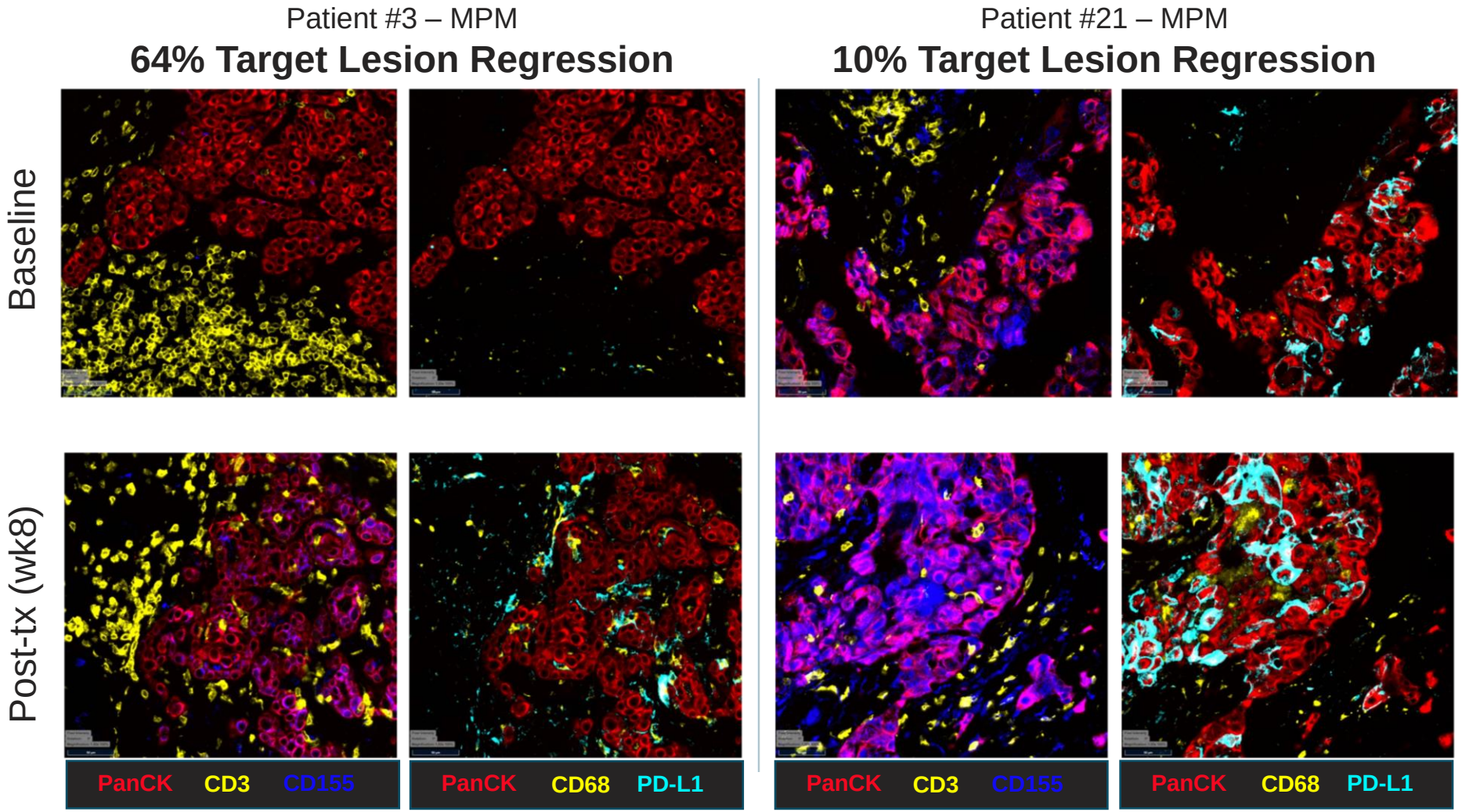
CPIs Expected to Improve Activity of TRuC-T Cells

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 MultiOmxy™ (Neogenomics)

MPM, Malignant Pleural/Peritoneal Mesothelioma; CPI, Checkpoint Inhibitor

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Expanding the Base

Innovating the Next Generation of TRuCs

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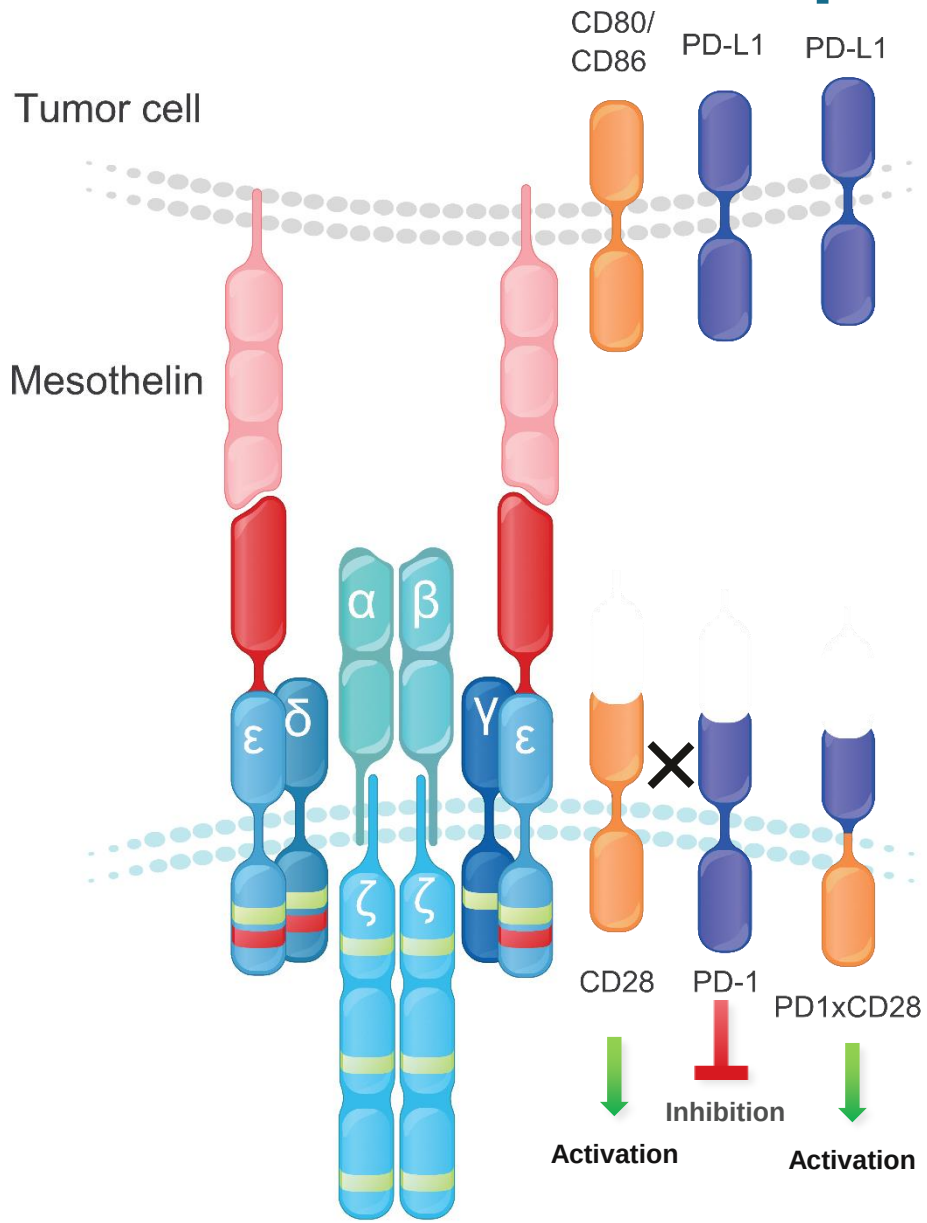
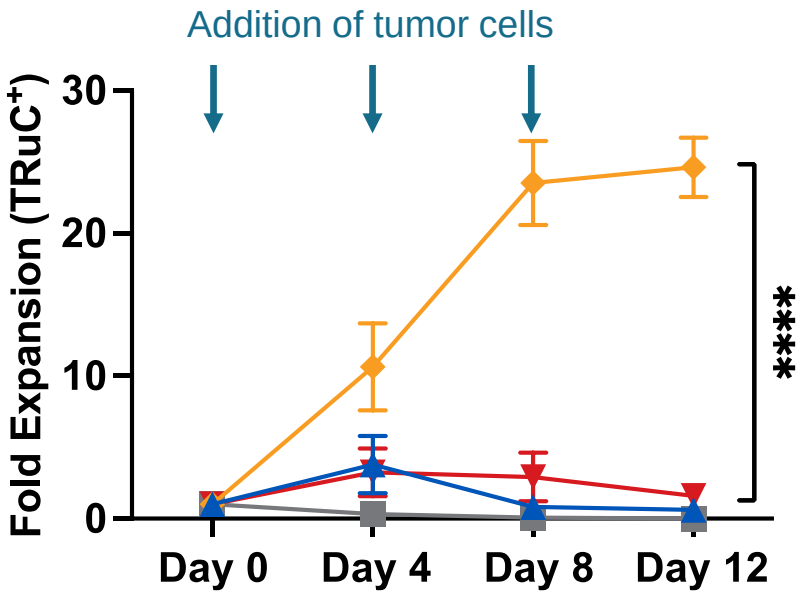
Enhancing gavo-cel with a PD-1:CD28 Switch Receptor

- 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

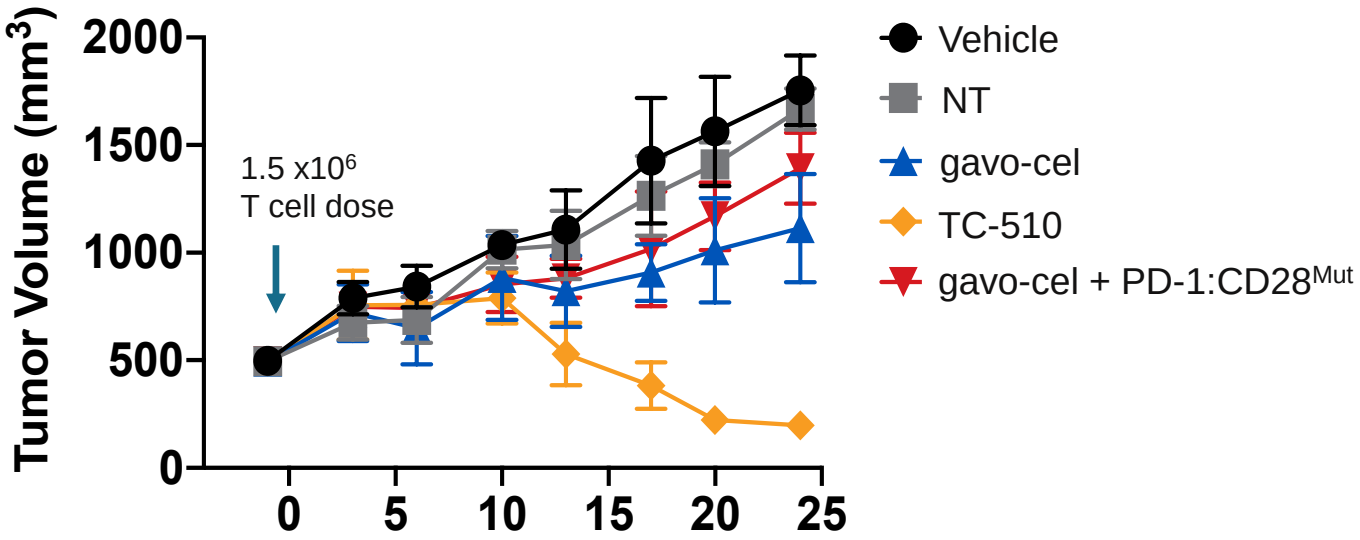


Against Tumors with High PD-L1 Expression, TC-510 Shows Enhanced Proliferation and Superior Efficacy

Expansion upon Repeated Stimulation



Anti-Tumor Activity in Mouse Model



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

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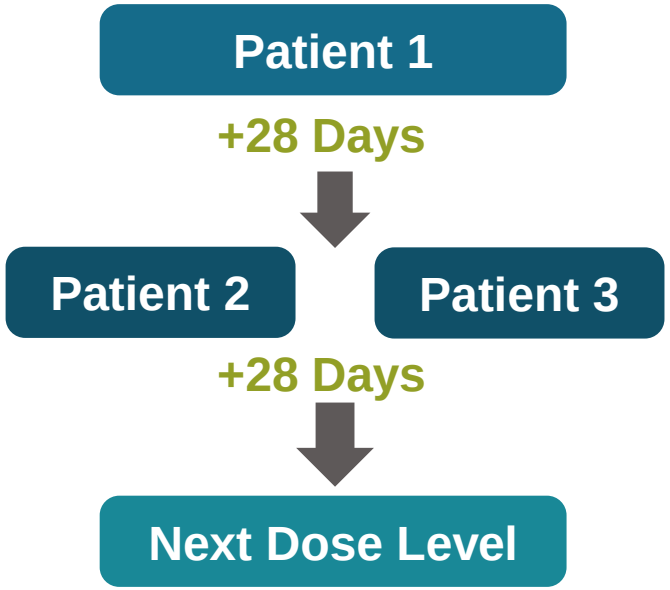
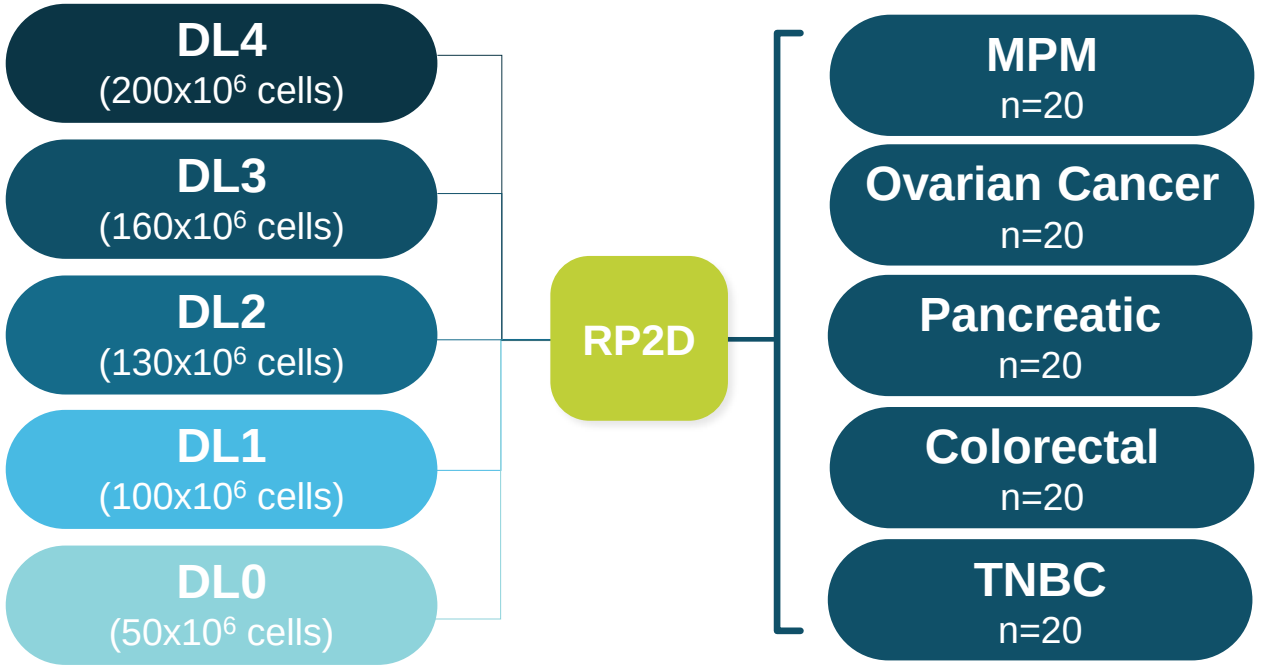
TC-510 Phase 1 Trial in MSLN+ Solid Tumors

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+

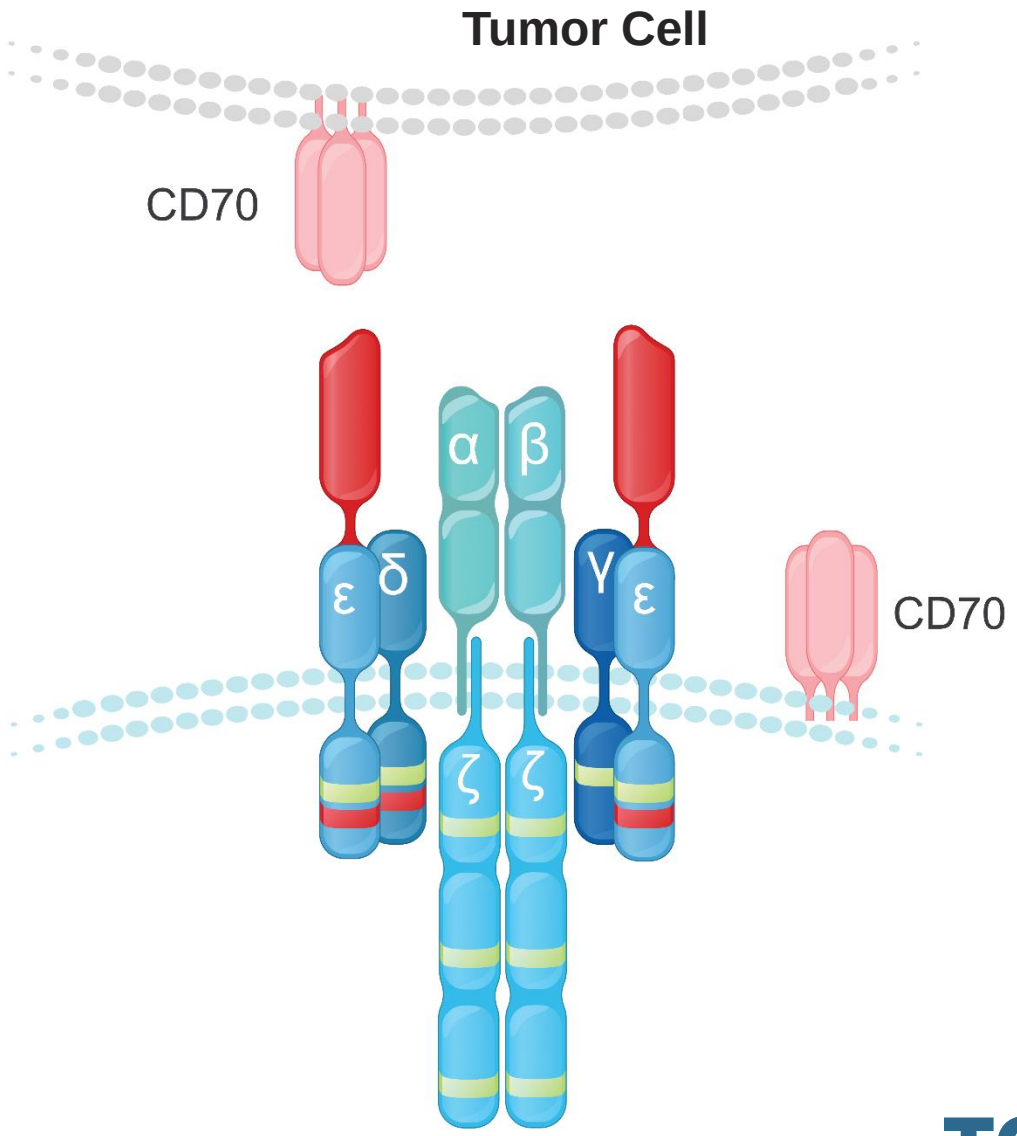
LD, Lymphodepletion; RP2D, Recommended Phase 2 dose; MPM, Malignant Pleural/Peritoneal Mesothelioma; TNBC, Triple Negative Breast Cancer; ORR, Overall Response Rate; DoR, Duration of Response; DCR, Disease Control Rate; SD, Stable Disease; PFS, Progression Free Survival; OS, Overall Survival

TCR2 THERAPEUTICS

CD70: Highly Attractive Target with an Innate Fratricide Challenge

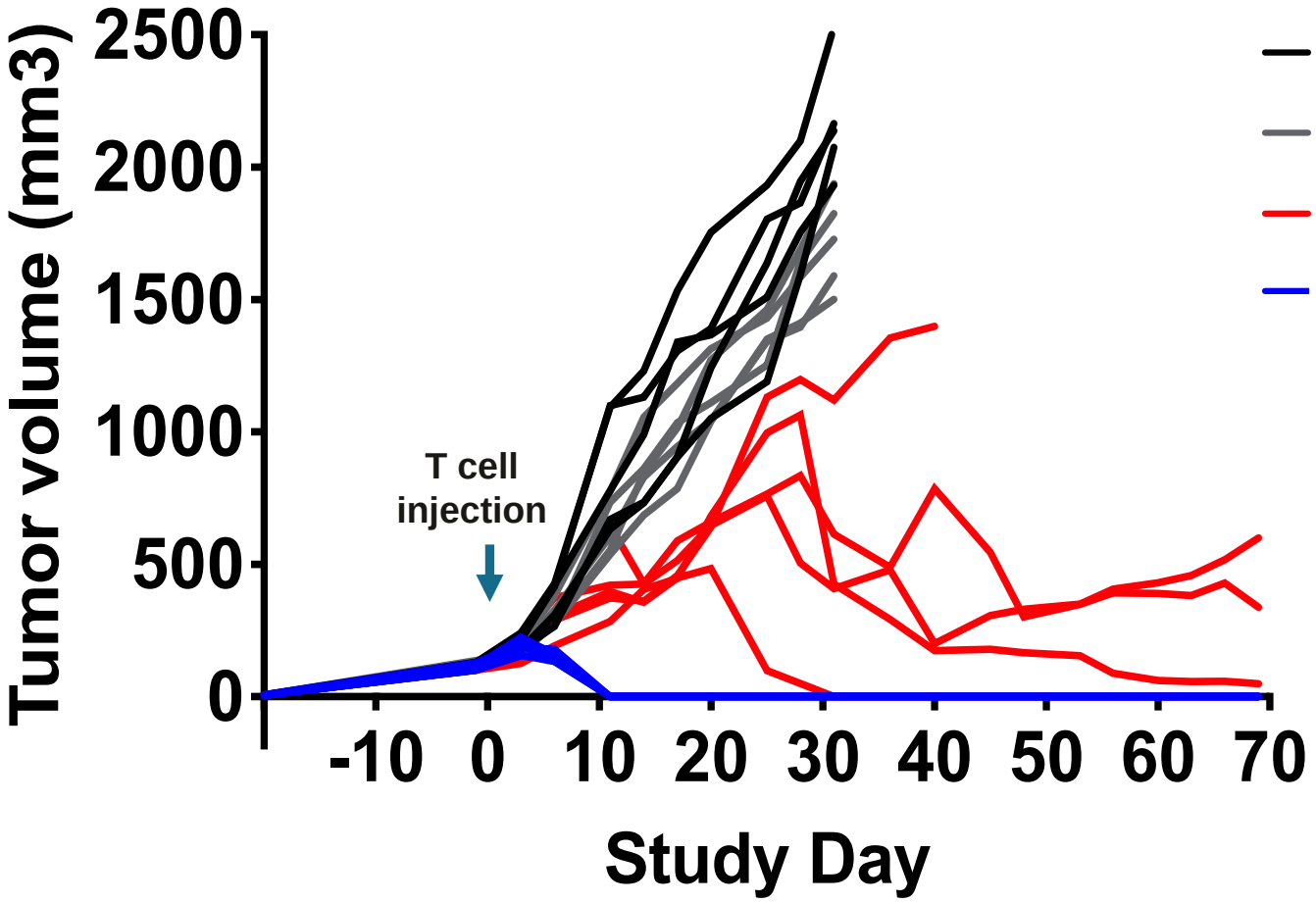
Up to 141,000 Patients Expressing CD70 in the US

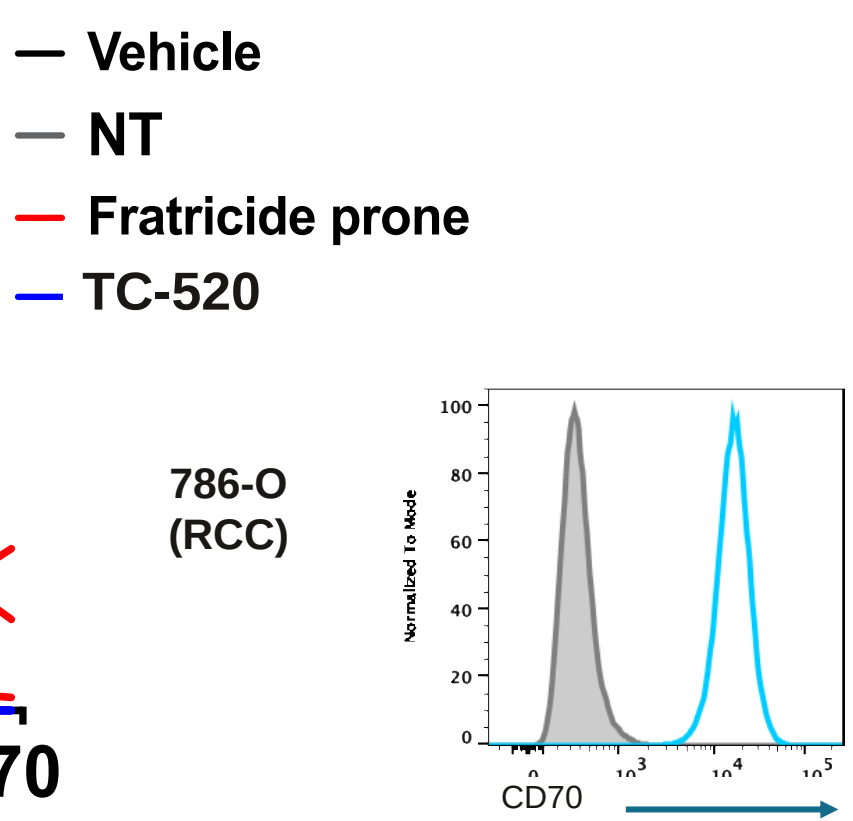
- Versatile tumor target: expressed in hematological malignancies (AML, lymphoma) and solid tumors (RCC, NSCLC, OC)
  - Expression in normal cells limited to a subset of activated T cells, B cells, and dendritic cells
  - Expression in activated T cells renders CD70-directed T cell therapies susceptible 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



AML, acute myeloid leukemia; RCC, renal cell carcinoma; NSCLC, non-small cell lung cancer; OC, ovarian cancer

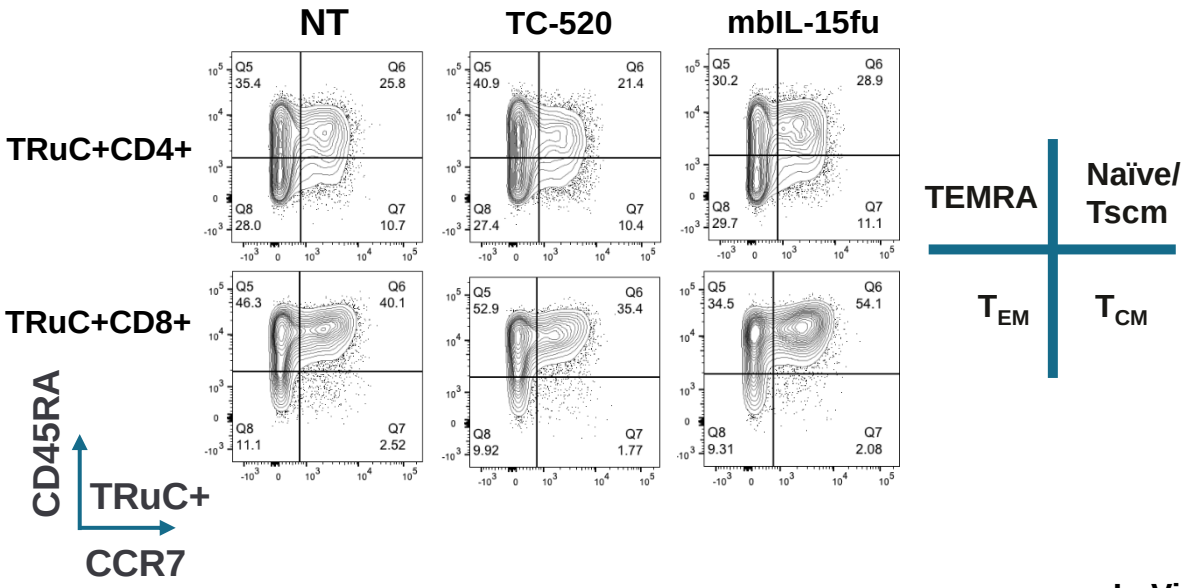
TC-520 Exhibits Potent and Persistent *In Vivo* Efficacy

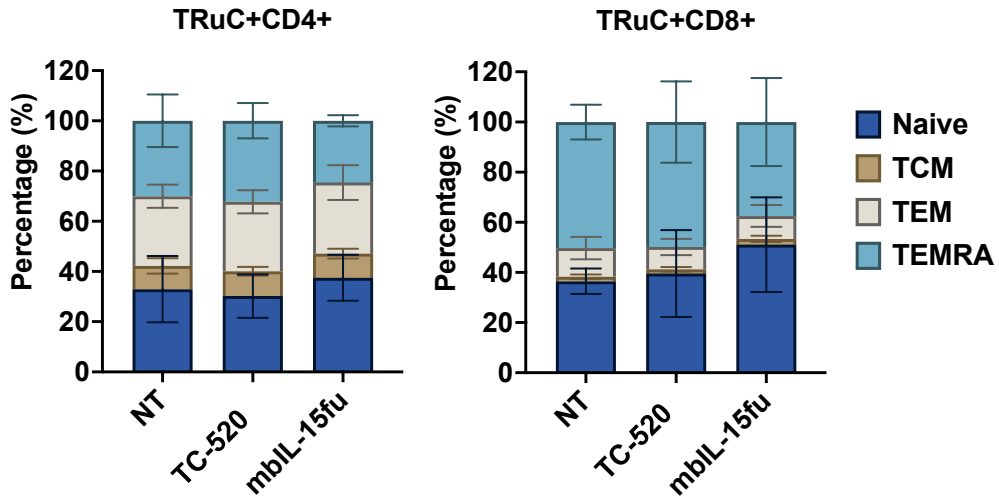


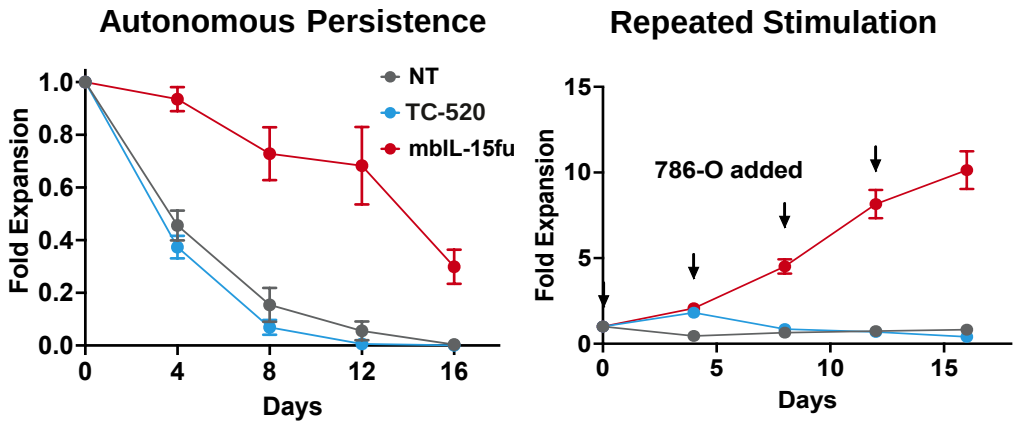


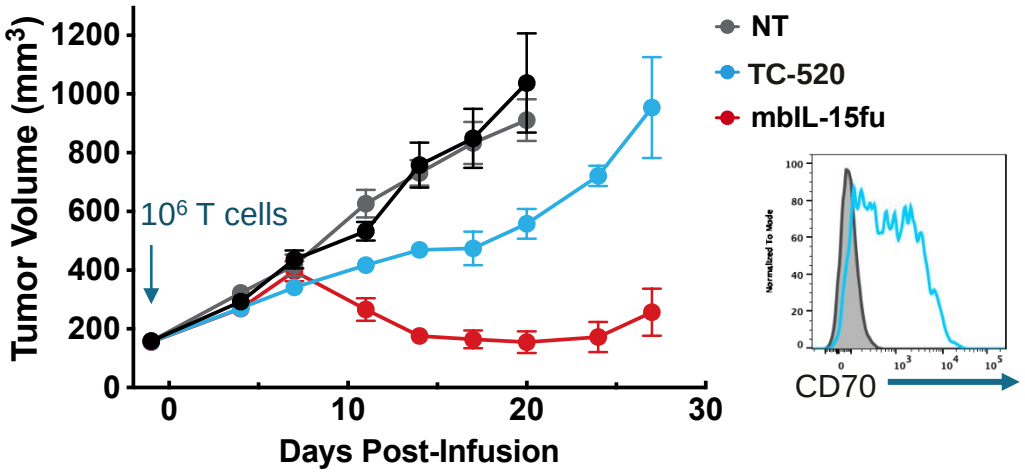
RCC, renal cell carcinoma

IL-15 Enhancement Improves TC-520 Phenotype and Function







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