TCR² THERAPEUTICS

POWERING T CELLS FOR
**CANCER CURES**

# Presentation of Clinical Data from First Cohort of TC-210 Patients

*Trial ongoing with additional patients enrolled and treated*

# 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 1/2 clinical study of TC-210 and our planned Phase I clinical trial of TC-110, our expectations for the safety and efficacy of our product candidates, including TC-210 and TC-110, compared to current T-cell therapy approaches, and our expectations regarding the estimated patient populations and related market opportunities in TC-210's and TC-110's targeted indications, 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 1/2 clinical trial of TC-210 and the planned Phase 1 clinical trial of TC-110; the risk that the results from the Phase 1/2 clinical trial of TC-210 will not support further development and marketing approval; the risk that we may be unable to gain approval of TC-210 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, 2019, as filed with the SEC on March 30, 2020, as updated in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, as filed with the SEC on May 14, 2020, 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. We have filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission ("SEC") on March 6, 2020, as amended on March 30, 2020, and declared effective by the SEC on April 28, 2020, for the offering to which this presentation relates. A preliminary prospectus supplement relating to, and describing the terms of, the offering will be filed with the SEC. Before you invest, you should read the registration statement, the preliminary prospectus, the documents that we have filed with the SEC that are incorporated by reference into the registration statement, and the other documents we have filed with the SEC for more complete information about us and the offering. You may get these documents for free by visiting EDGAR on the SEC website at www.sec.gov. Alternatively, copies of the preliminary prospectus supplement and the accompanying prospectus relating to this offering can be obtained from Jefferies LLC, Attention: Equity Syndicate Prospectus Department, 520 Madison Avenue, 2nd Floor, New York, NY 10022, by telephone at (877) 821-7388, or by email at prospectus_department@Jefferies.com; SVB Leerink LLC, Attention: Syndicate Department, One Federal Street, 37th Floor, Boston, MA 02110, by telephone at 800-808-7525, ext. 6218 or by email at syndicate@svbleerink.com; Piper Sandler & Co., Attn: Prospectus Department, 800 Nicollet Mall, Minneapolis, Minnesota 55402, by telephone at 800-747-3924 or by email at prospectus@psc.com; or BMO Capital Markets Corp., Attention: Equity Syndicate Department, 3 Times Square, 25th Floor, New York, NY 10036, by telephone at (800) 414-3627 or by e-mail at bmoprospectus@bmo.com. The final terms of the offering will be disclosed in a final prospectus supplement to be filed with the SEC.

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# Introduction

## Garry Menzel, PhD

Chief Executive Officer

# Key Takeaways from Our First Cohort of TC-210 Patients

## Clinical Trial Overview

- Data on first 5 patients: 4 patients with mesothelioma, 1 with ovarian cancer
- Single infusion of TC-210 TRuC-T Cells ($5x10^7$ cells/$m^2$)
- Lymphodepletion
  - Fludarabine (30 mg/$m^2$/day x4)
  - Cyclophosphamide (600 mg/$m^2$/day x3)

## Key Clinical Findings

- **Screening**: 48% patients eligible
- **Manufacturing**: 100% success rate
- **Safety**: Manageable toxicity, no neurotoxicity or on-tumor, off-target toxicities
- **Translational**: Demonstrated T cell expansion and cytokine production
- **Clinical**: ORR 40%, 2 unconfirmed RECIST PRs, Disease Control Rate (DCR) 100%

# Mesothelin Is an Excellent Solid Tumor Target

## Expression Patterns

**Mesothelin** is **highly expressed** on tumors

Lower expression in normal tissue, confined to mesothelium in pleura, peritoneum and pericardium

***No expression in vital organs***

## Clinical Data

**Target validation from competitor programs**, including:

Memorial Sloan Kettering Cancer Center

NOVARTIS

Penn Medicine

BAYER

Bristol-Myers Squibb

CAR-T

ADC

## Clinical Need

**Up to 80,000**

potentially addressable U.S. patients in TC-210's lead indications

***Overexpression linked to worse outcomes***

# Mesothelin Solid Tumors Represent A Significant Market

| Malignant Pleural Mesothelioma | Cholangiocarcinoma | Ovarian Cancer | NSCLC |
|---|---|---|---|
|   |   |   |   |
| Market Opportunity: ~$700M | Market Opportunity: ~$800M | Market Opportunity: ~$1.6B | Market Opportunity: ~$1.6B |

**Fast Track Potential**

**Percent of Patients with Mesothelin Surface Expression**

**Patients with Mesothelin Surface Expression (U.S., 2019)**

**~$5.0B consensus global peak sales of TC-210**

Consensus based on average analyst estimates covering the company

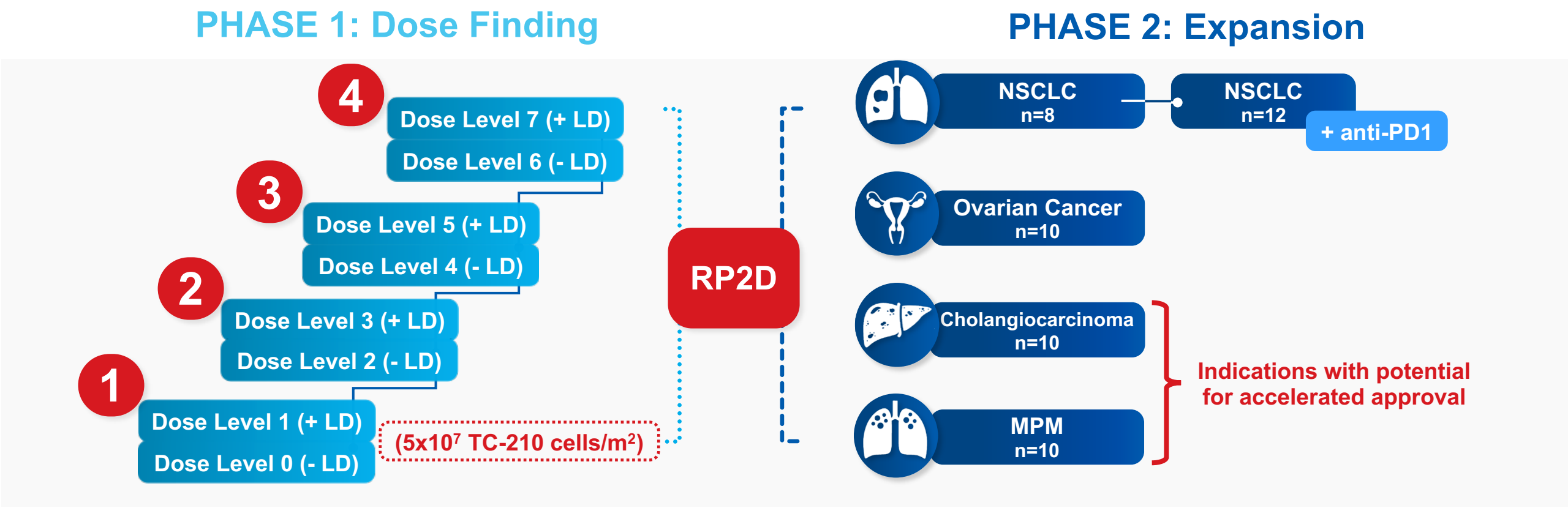
NSCLC, Non-small cell lung cancer

Refs: Inaguma 2017, SEER Statistics, Morello 2016

# TC-210 Clinical Trial Review

Alfonso Quintás-Cardama, MD
Chief Medical Officer

# Ongoing TC-210 Phase 1/2 Trial in MSLN+ Cancers

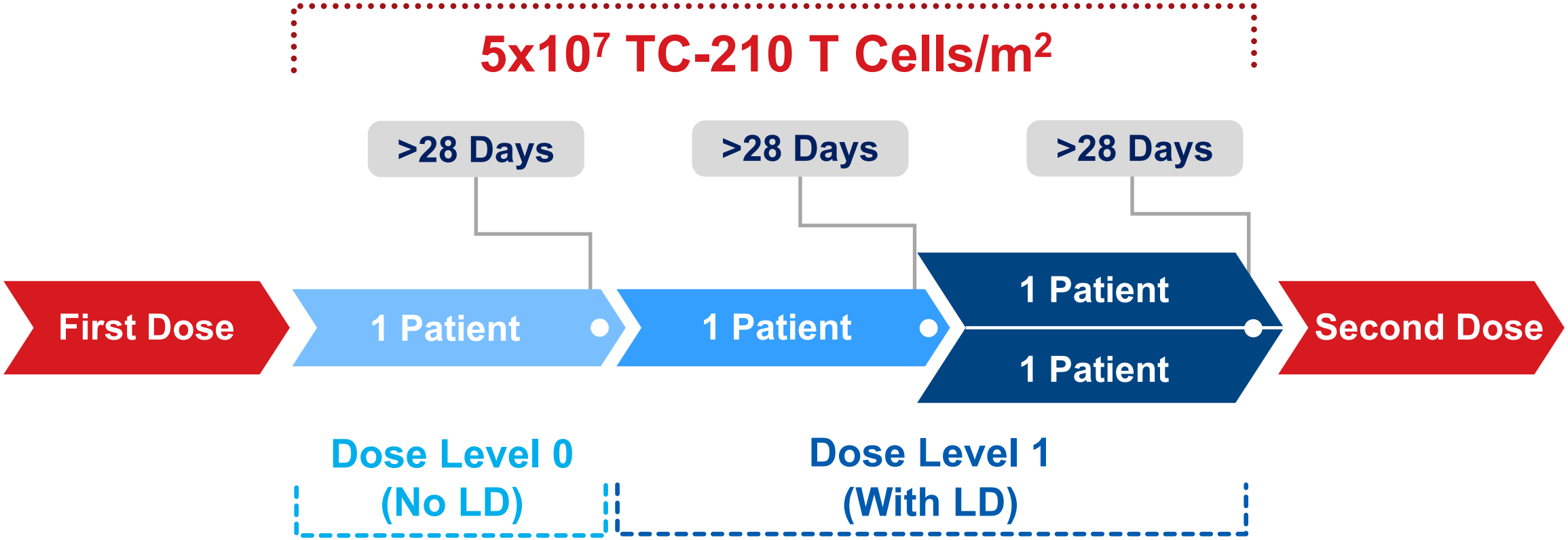



**(– LD) Cohorts = 1 patient**
**(+ LD) Cohorts = 3 patients**

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

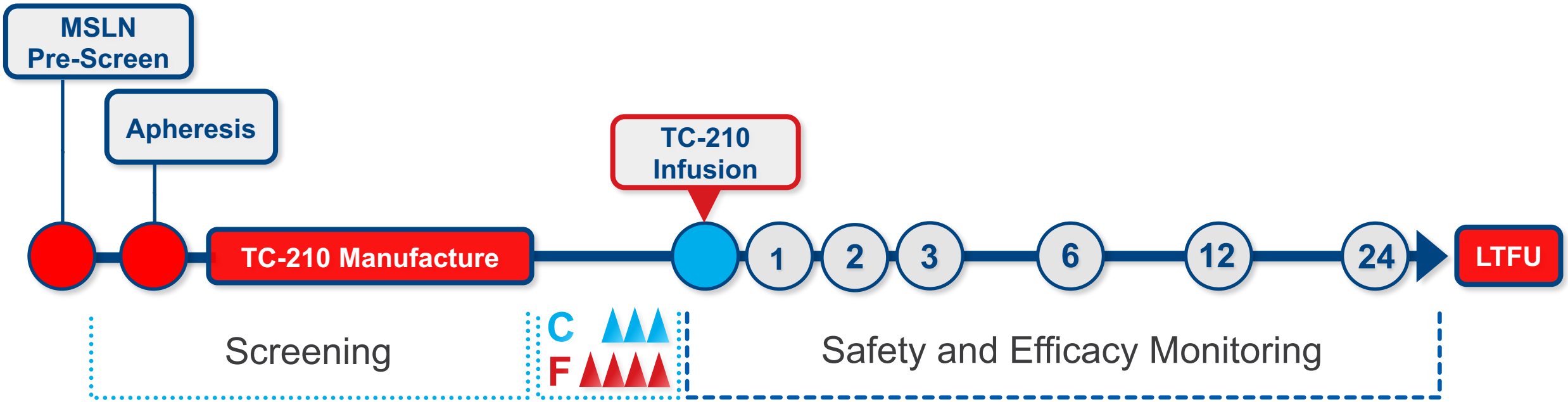
# Enrollment Rules During Phase 1

*Modified 3+3 Dose Escalation*




LD: Lymphodepletion

# TC-210 Study: Patient Flow




## Mesothelin Expression

- Central lab (Roche/Ventana)

## Lymphodepletion Regimen

- Fludarabine (F): 30 mg/m$^2$ x4
- Cyclophosphamide (C): 600 mg/m$^2$ x3

## TC-210 Administration

- Overnight observation

## Clinical Trial Sites

- Sarah Cannon Research Institute
- University of Texas MD Anderson Cancer Center
- National Cancer Institute
- University of Pennsylvania
- Memorial Sloan Kettering Cancer Center

MSLN: mesothelin; LTFU: long term follow-up

# TC-210 Phase 1 Dose Escalation: Objectives

## Primary

- Safety (Establish the RP2D)

## Secondary

- ORR (CR + PR) according to RECIST v1.1
- DCR (ORR + SD)
- Duration of response
- Survival (PFS, OS)

## Exploratory

- Expansion, persistence, phenotype, functionality of TC-210 T-cells
- Serum cytokine levels
- Immunogenicity

# TC-210 Phase 1 Dose Escalation: Eligibility Criteria

## Key Inclusion Criteria

- ≥ 18 years of age
- Adequate Performance Status and organ function
- Pathologically confirmed MPM, NSCLC, ovarian cancer, or cholangiocarcinoma
- Must have received at least 1 systemic standard of care therapy for metastatic and/or unresectable disease
  - **Mesothelioma**: platinum-based therapy
  - **NSCLC**: if actionable mutation must have received appropriate FDA approved agent (e.g. osimertinib); if no actionable mutation, must have received a currently approved frontline regimen
  - **Ovarian cancer**: post frontline therapy; post PARP inhibitor if BRCA1/2 mutated
  - **Cholangiocarcinoma**: post one systemic regimen (frontline if patient refuses standard frontline therapy)
- Measurable disease per RECIST v1.1
- **MSLN expression by IHC (Roche Ventana): 2+ or 3+ in ≥ 50% viable tumor cells**

# Pre-Screening, Enrollment and Manufacturing Activity

- MSLN expression above enrollment cutoff in ~50% of screened patients
- Products meeting protocol specifications have been successfully manufactured for all enrolled patients
- Consistent transduction efficiency (mean 43%)

## Mesothelin Expression Cut-Off

- 2+ or 3+ in ≥ 50% viable tumor cells

| | |
|---|---|
| **Patients Pre-Screened** | 79 |
| **Tumor Samples Resulted** | 62 |
| **MSLN 2+/3+ in ≥ 50% viable tumor cells n (%)** | 30 (48) |
| **Patients Enrolled** | 18 |
| **Patients Apheresed** | 14 |
| **Patients Manufactured** | 12 |

# Patient Characteristics

| Characteristics | N = 5 |
|---|---|
| Median age, years (range) | 61 (36-74) |
| Cancer diagnosis | |
| Mesothelioma | 4 (2 peritoneal, 2 pleural) |
| Ovarian cancer | 1 |
| Median No. of prior therapies (range) | 5 (3-9) |
| ≥4 prior therapies, No. (%) | 3 (60) |
| Prior ICI therapy, No. (%) | 3 (60) |
| Prior anti-MSLN directed therapy, No. (%) | 1 (20) |
| Transduced cells infused $x10^7$, Median (range) | 9.09 (7.54 – 10.36) |
| No. awaiting infusion (manufactured product) | 6 |

ICI: immune checkpoint inhibitor; MSLN: mesothelin

# Summary of Grade ≥3 Treatment Emergent Adverse Events

| Adverse Event | N = 5 (%) |
|---|---|
| **Hematologic** | |
| Neutropenia | 4 (80) |
| Lymphopenia | 5 (100) |
| Thrombocytopenia | 1 (20) |
| **Adverse Events of Special Interest** | |
| ***On Target / On Tumor*** | |
| CRS* | 1 (20) |
| Neurotoxicity | 0 |
| ***On Target / Off Tumor*** | |
| Pericarditis / Pericardial effusion | 0 |
| Pleuritis / Pleural effusion | 0 |
| Peritonitis / Ascites | 0 |
| ***Infection / Inflammation*** | |
| Pneumonitis* | 1 (20) |
| Sepsis* | 1 (20) |

*Occurred in same patient

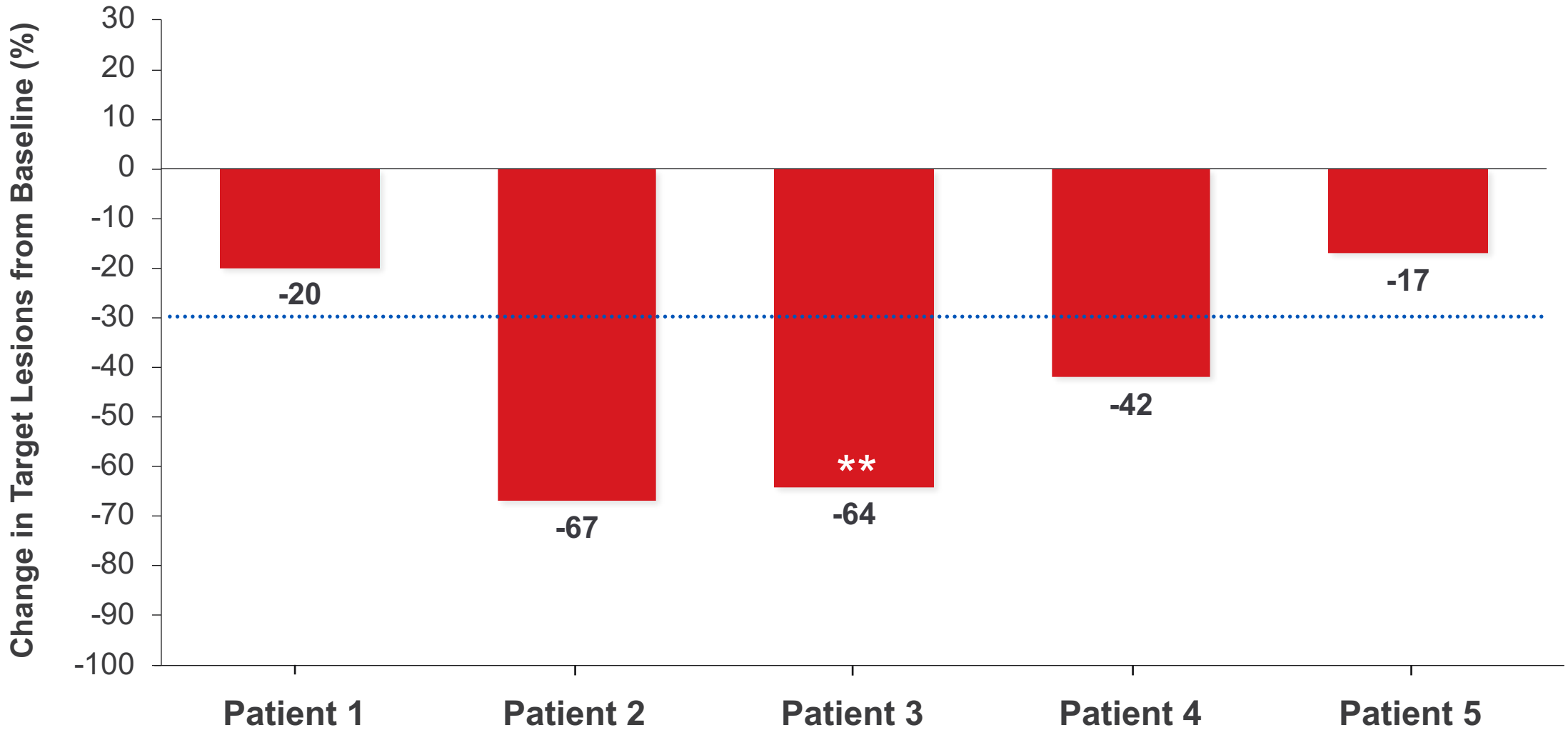
# RECIST v1.1 Response Assessment Summary

| Patients | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| **Age/Sex** | 61/M | 74/M | 52/F | 36/M | 70/F |
| **Diagnosis** | MPM | MPM | MPM | MPM | Ovarian Ca |
| **MSLN 2+/3+ (% of tumor cells)** | 90 | 60 | 73 | 95 | 55 |
| **No. Prior Rx** | 8** | 3 | 3 | 9 | 6 |
| **Bridging Therapy** | None | Pemetrexed/ Cisplatin | Pemetrexed/ Carboplatin | None | Liposomal doxorubicin |
| **LD Chemo** | No | Yes | Yes | Yes | Yes |
| **TC-210 dose** | $5x10^7/m^2$ | $5x10^7/m^2$ | $5x10^7/m^2$ | $5x10^7/m^2$ | $5x10^7/m^2$ |
| **Best Target Lesion Response** | SD | PR | PR | PR | SD |
| **Best RECIST v1.1 Response** | SD | PR* | SD | PR*+ | SD |

*Unconfirmed
** Received anti-mesothelin ADC
+ Subject to independent central review

# Tumor Regression Observed in All Patients with TC-210

*Overall Response Rate 40%, Disease Control Rate 100%*




** New Lesion at Month 6

# Early Efficacy Case Study: Patient 2

*Partial Response (RECIST v1.1), Significant Tumor Regression (67%), Complete Metabolic Response*

**74-year-old male, epithelioid pleural mesothelioma**

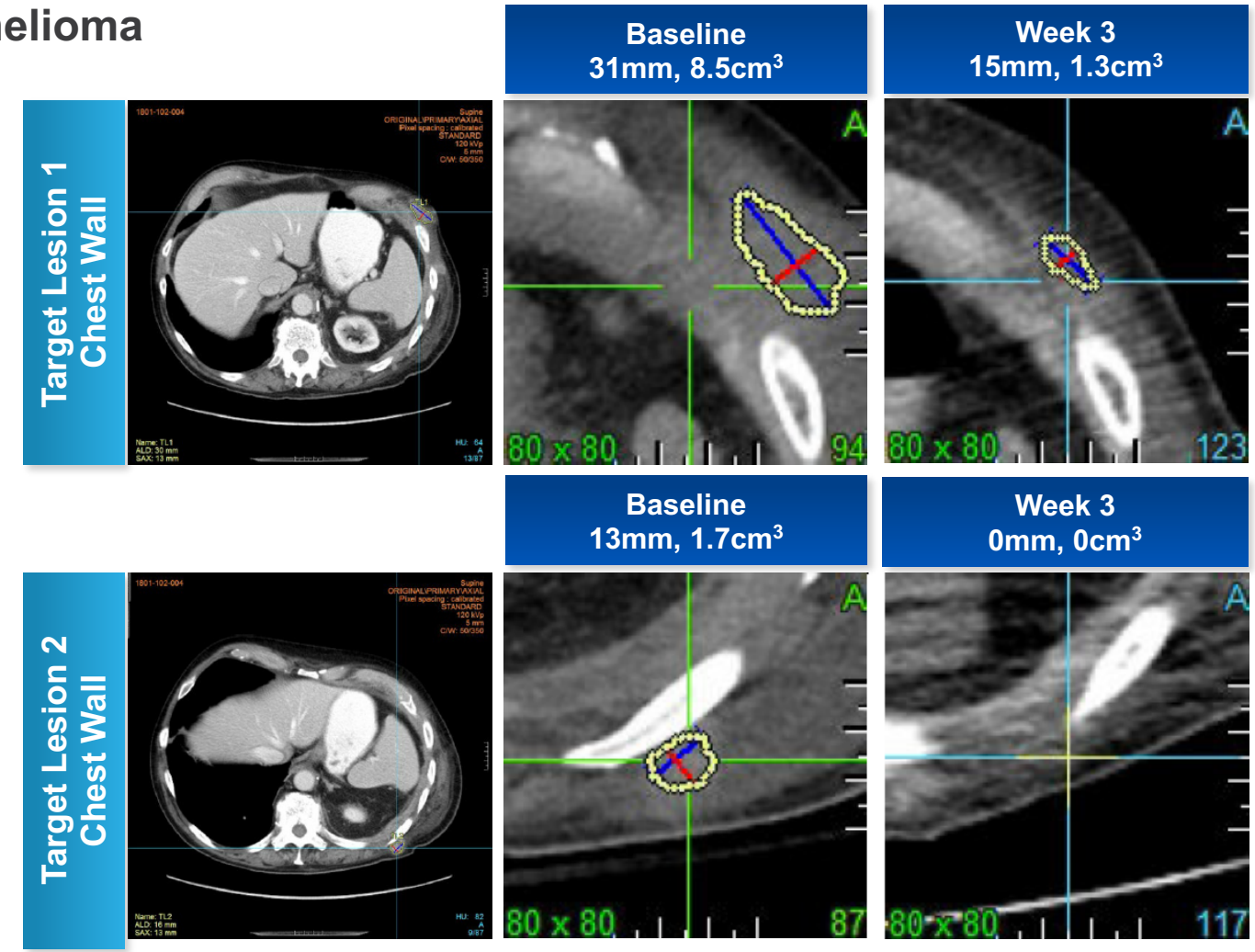
- Extensive surgery Feb 2018 ➡ PD
- Pembrolizumab Sep 2018 ➡ PD
- Carboplatin/pemetrexed Apr 2019 (x4) ➡ PD

## Enrolled in TC-210 Clinical Trial Study

- **September 2019**: Lymphodepletion with Flu/Cy followed by $5x10^7/m^2$ TC-210 T cells

## Response at Week 3 Post TC-210

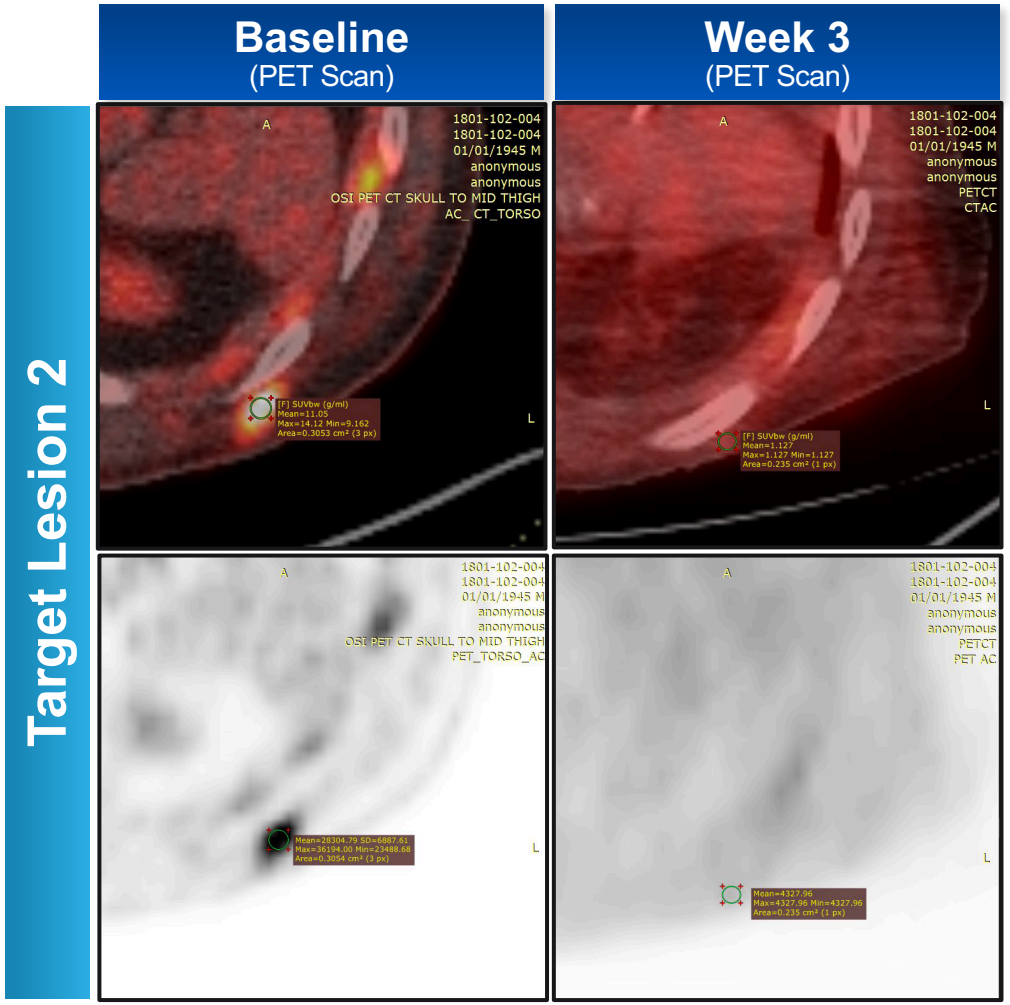
- Target Lesions: **PR**
- Overall: **PR***




*Unconfirmed

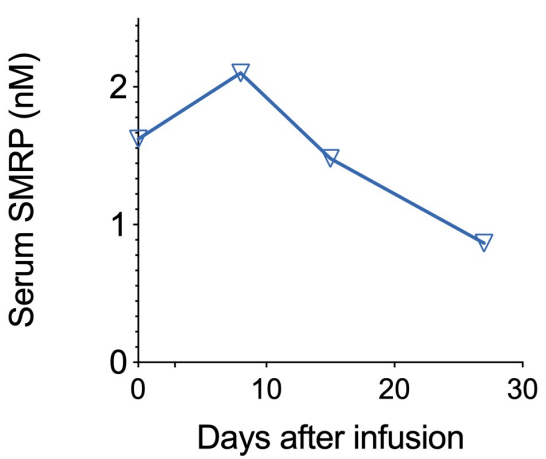
# Early Efficacy Case Study: Patient 2

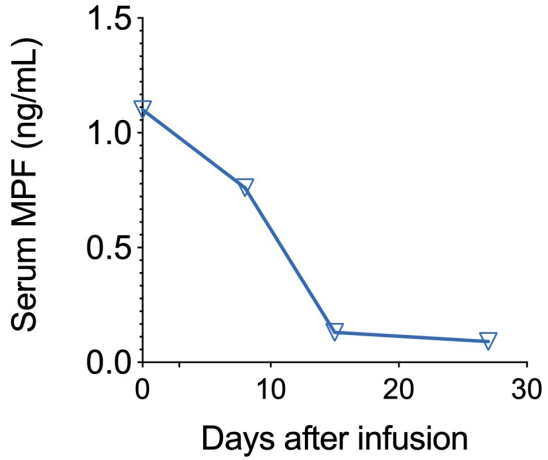
**74-year-old male, epithelioid pleural mesothelioma**




**Complete Metabolic Response**

## Soluble Mesothelin & MPF



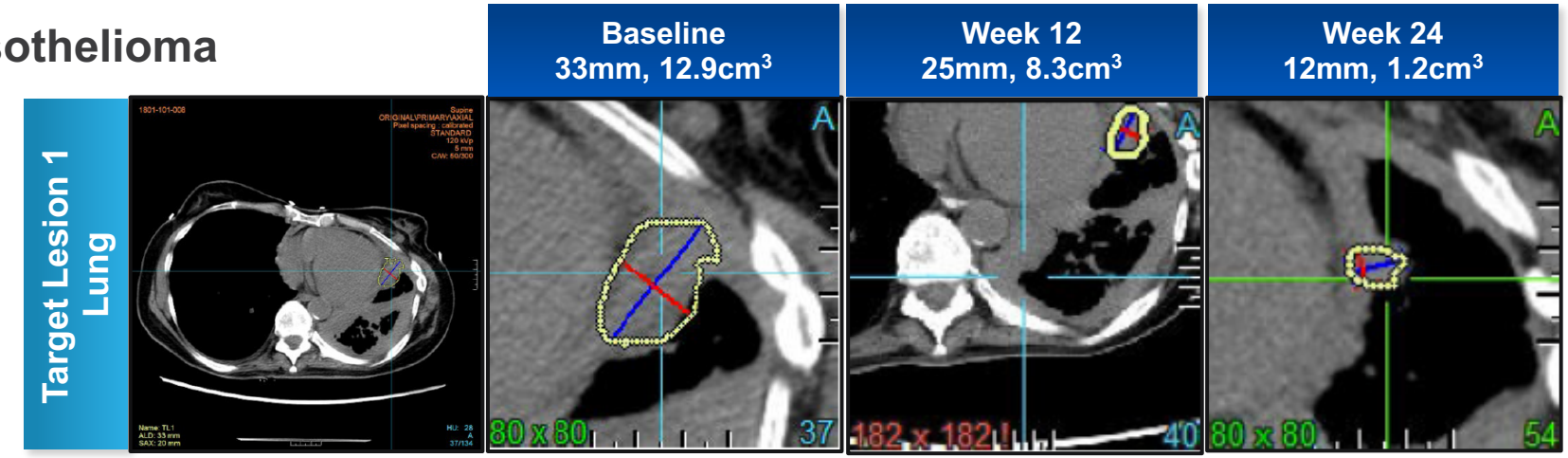



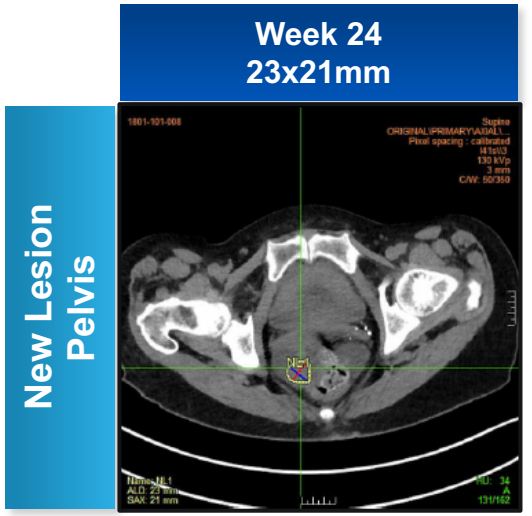
# Early Efficacy Case Study: Patient 3

*Significant Tumor Regression (64%)*

## 52-year-old female, epithelioid mesothelioma

- Diagnosed Aug 2015
- Left parietal pleurectomy
- Cisplatin/pemetrexed Oct 2015 ➡ **SD**
- Extensive cervical, mediastinal, abd/pelvic masses, bone metastases May 2019
- Carboplatin/pemetrexed July 2019 (x3) ➡ **PD**




## Enrolled in TC-210 Clinical Trial Study

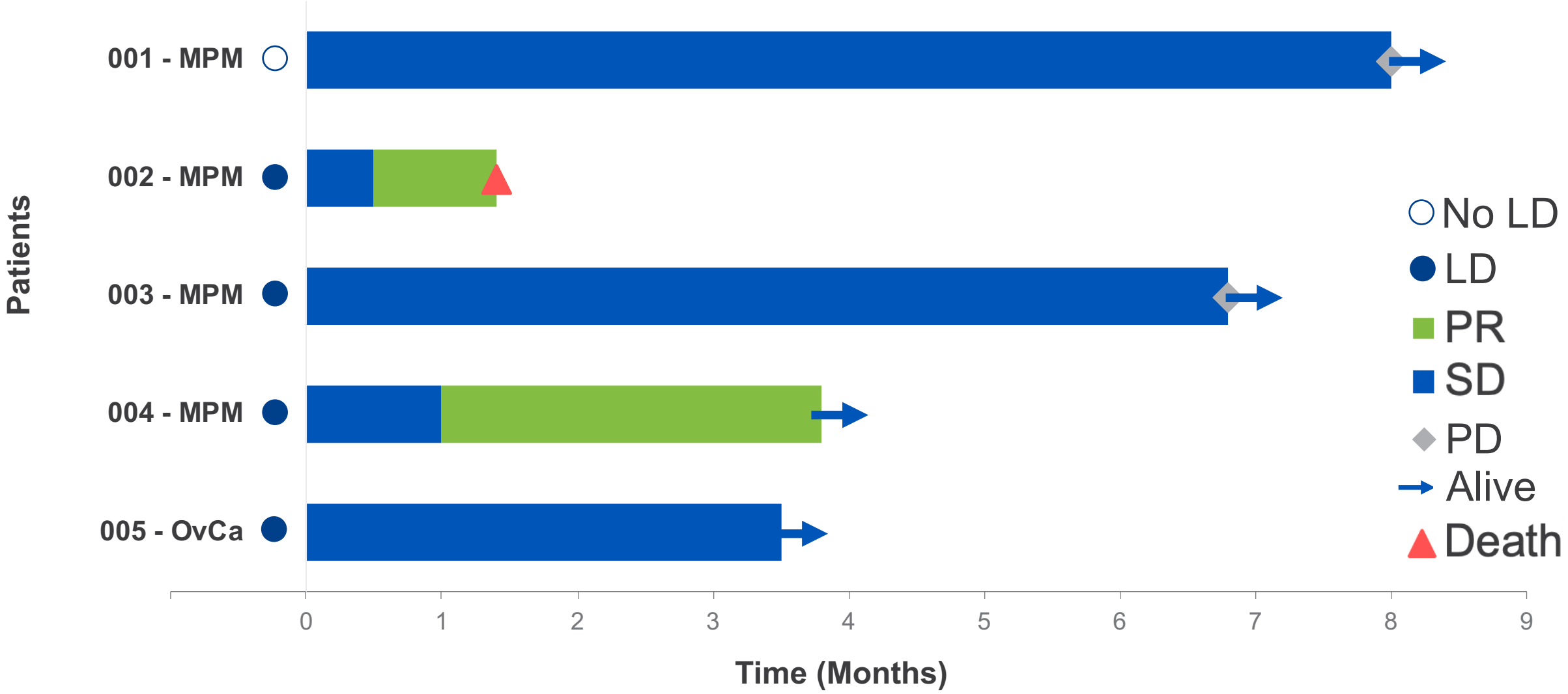
- **September 2019**: Lymphodepletion with Flu/Cy followed by $5x10^7/m^2$ TC-210 T cells

## Response at Month 6 Post TC-210

- Target Lesions: **PR**
- Overall: **PD** (new pelvic lesion)

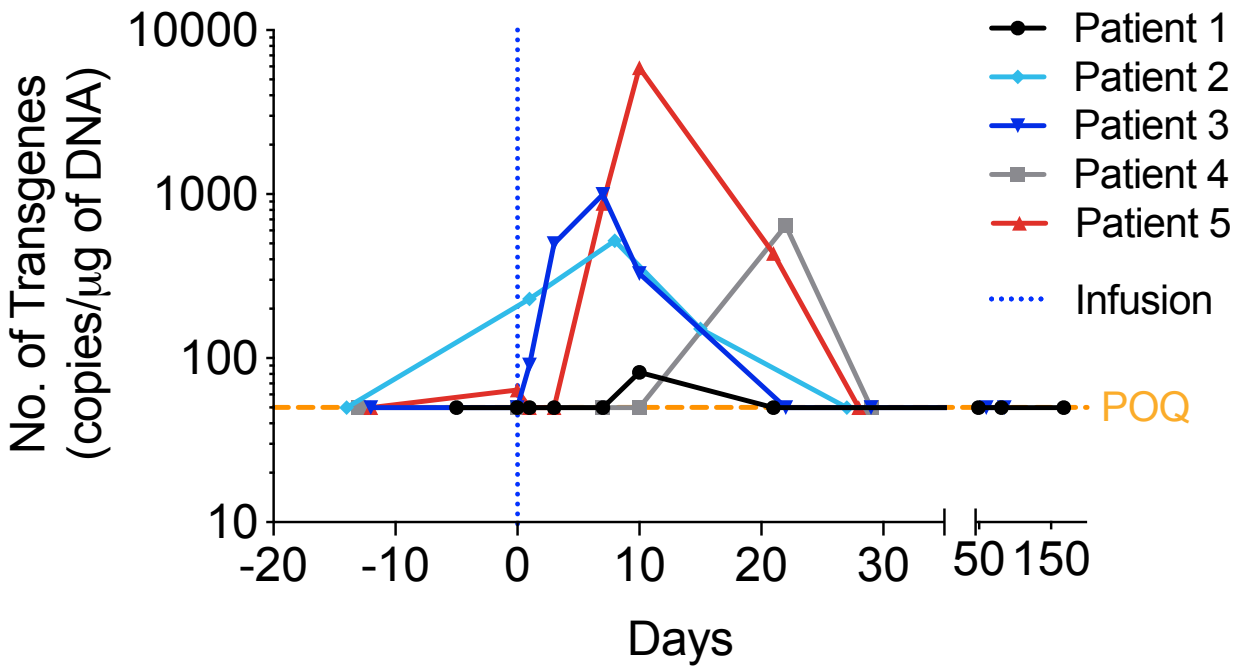
# Patient Response and Follow-Up

*Overall Response Rate 40%, Disease Control Rate 100%*

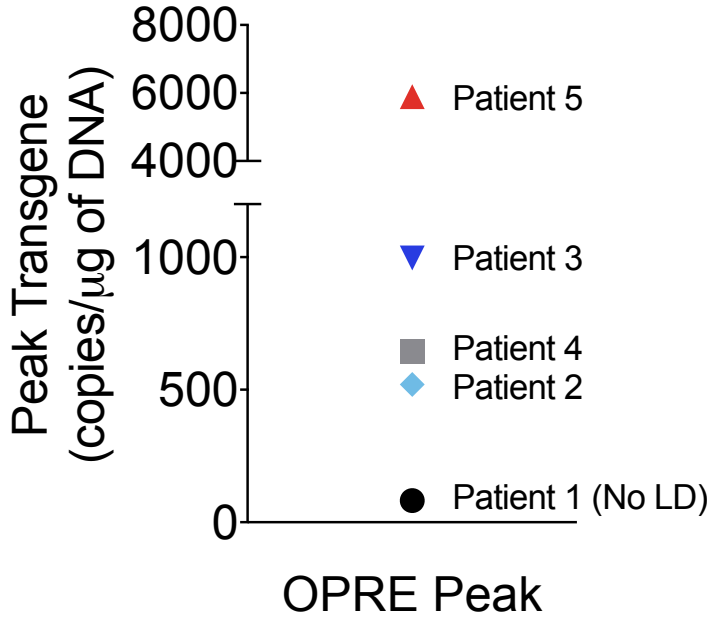


# TC-210 T Cell Expansion in Peripheral Blood by qPCR

## TC-210 Kinetics

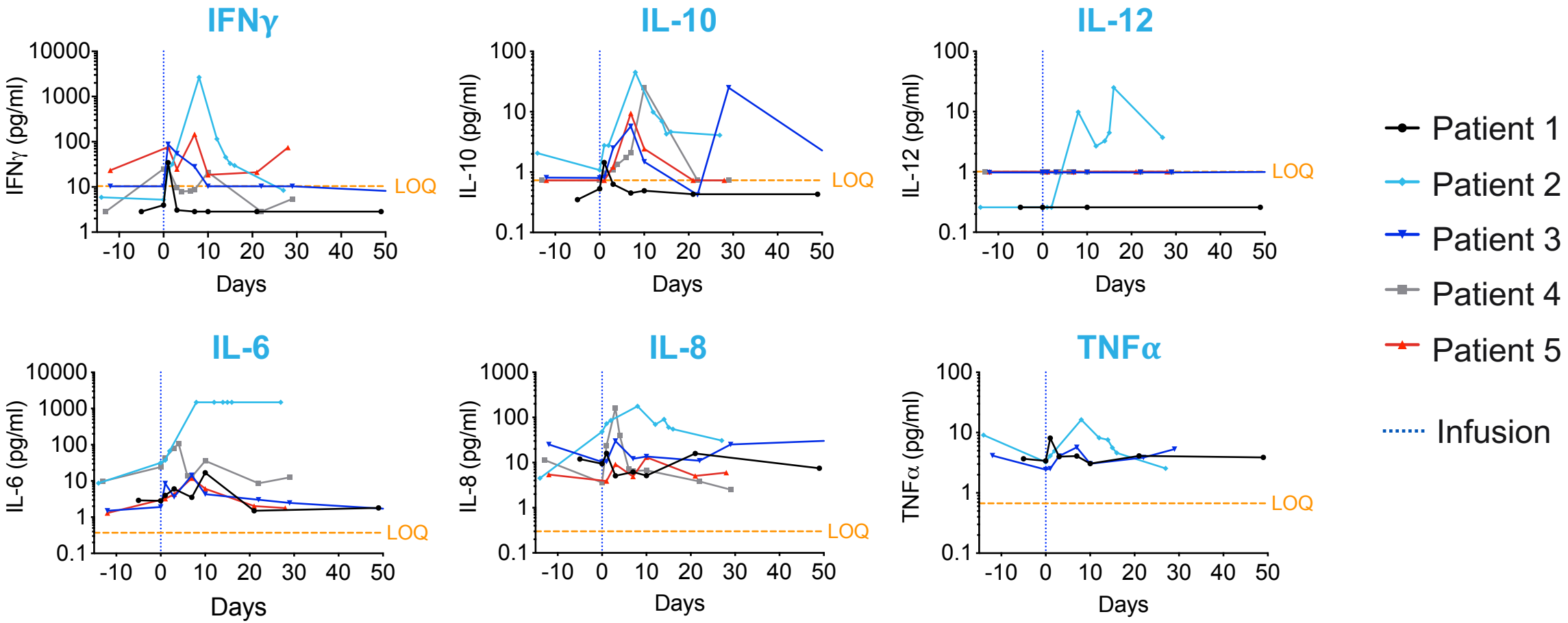



## Peak of TC-210 Expansion




- Expansion of TC-210 T Cells in peripheral blood observed in all patients
- Peak expansion occurred between days 7-22 post infusion
- Highest expansion was observed among patients receiving lymphodepletion

# Cytokine Levels in Peripheral Blood Following TC-210 Infusion

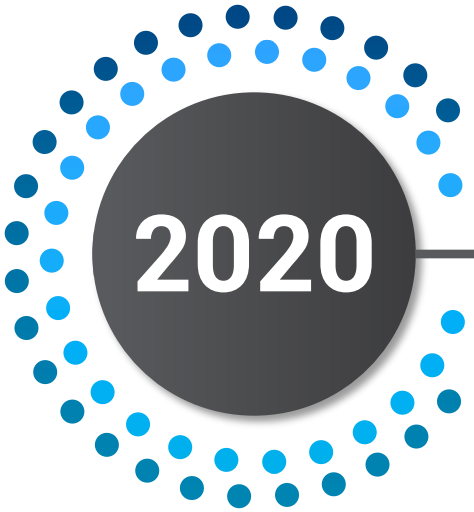



- TC-210 infusion increased cytokine levels in peripheral blood in all patients
- Higher levels were observed in Patient 2, who experienced grade 3 CRS

# TC-210: Summary and Future Direction

- **Encouraging data at first dose tested**
  - Consistent clinical benefit at first TC-210 T cell dose
  - Manageable safety profile
  - High rate of patient eligibility and 100% manufacturing success
- **Next steps**
  - Continue dose escalation until identification of RP2D
  - Initiate phase 2 portion of study, including TC-210 combination with anti-PD1 antibody
- **Additional data expected later in 2020**
  - Data on additional cohorts
  - Detailed translational data

# 2020 Company Milestones




## 2H20

### TC-210

**Phase 1 Follow-Up Update**

**Target**: Mesothelin

**Indications**: Ovarian Cancer, NSCLC, MPM, Cholangiocarcinoma

**Endpoints**: Safety, Efficacy & Translational Data
(i.e. infiltration, persistence, cytokines, expansion, phenotype)

## 2H20

### TC-110

**Phase 1 Interim Update**

**Target**: CD19

**Indications**: aALL, DLBCL, NHL

**Endpoints**: Safety, Efficacy & Translational Data
(i.e. persistence, cytokines, expansion, phenotype)

## 2020

### New Targets

Broaden reach with unique binders in hematologic cancers and solid tumors

\+

### Enhancements

Dual TRuCs, PD-1 axis and other enhancements to combat the tumor microenvironment

\+

### Allogeneic TRuCs

"Off-the-shelf" to simplify manufacturing and reduce costs of therapy

**Active Partnering Discussions as Clinical Data Matures**

# Early Clinical Validation of TRuC-T Cell Platform Strengths

Faster T-Cell Migration

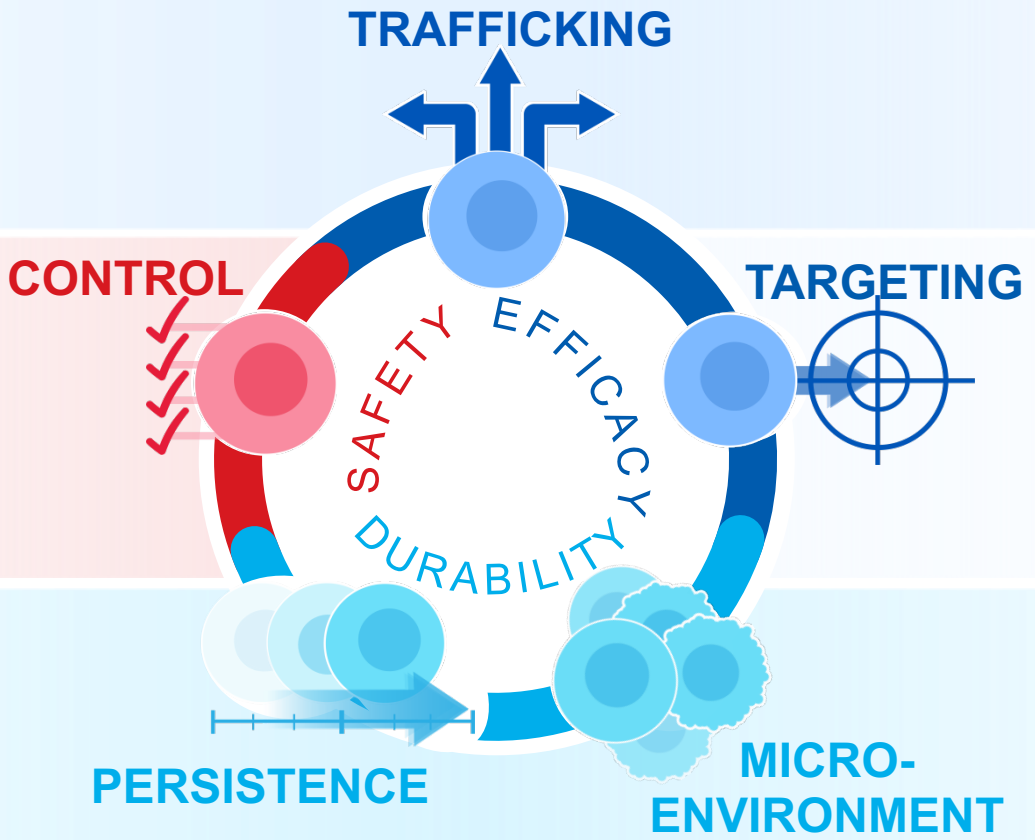
Increased Homing Receptors

Reduced Cytokine Release

Preferential Killing

Long-Lasting Anti-Tumor Activity

Enhanced Metabolism



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**Thank You**