

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 8-K

**CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Act of 1934**

**Date of Report (Date of earliest event reported):
September 28, 2022**

TCR² THERAPEUTICS INC.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

001-38811
(Commission
File Number)

47-4152751
(I.R.S. Employer
Identification Number)

**100 Binney Street, Suite 710
Cambridge, Massachusetts**
(Address of principal executive offices)

02142
(Zip Code)

Registrant's telephone number, including area code: (617) 949-5200

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13d-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	TCRR	The Nasdaq Stock Market, LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On September 28, 2022, TCR² Therapeutics Inc. (the “Company”) issued a press release titled “gavo-cel Continues to Demonstrate Clinical Benefit in Solid Tumors with Additional RECIST Responses in Ovarian Cancer and Mesothelioma.” A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information under this Item 7.01, including Exhibit 99.1 attached hereto, is being furnished herewith and shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

Phase 1 Topline Results

On September 28, 2022, the Company announced positive topline results from the Phase 1 portion of the Company’s gavo-cel Phase 1/2 clinical trial for mesothelin-expressing solid tumors, with some patients still being monitored for clinical response or stable disease.

As of the September 9, 2022 data cutoff, 32 patients (including 23 mesothelioma, eight ovarian cancer and one cholangiocarcinoma) had received a single gavo-cel infusion in the Phase 1 portion of the clinical trial. The patients were heavily pretreated with a median of five prior lines of therapy, including immune checkpoint inhibitors in 66% of patients and mesothelin-directed therapies in 19% of patients. Following identification of a dose-limiting toxicity (DLT) at dose level (DL) 5 (5x10⁸ cells/m² following lymphodepletion) in September 2021, the study proceeded to a dose de-escalation portion, first at DL3.5 (3x10⁸ cells/m² following lymphodepletion) using a split-dosing approach, and subsequently at DL3 (1x10⁸ cells/m² following lymphodepletion) which was declared the recommended Phase 2 dose (RP2D). No new DLTs were observed.

gavo-cel demonstrated a disease control rate (DCR) of 77%, which is defined in the Phase 1 portion of the trial as a response or sustained stable disease for at least 3 months post infusion. As measured by blinded independent central review (BICR), 28 of the 30 (93%) patients evaluable for efficacy experienced tumor regression of their target lesions, ranging in magnitude from 4% to 80%. Eight patients experienced target lesion regression greater than 30%, six of whom (four with mesothelioma and two with ovarian cancer) achieved a partial response (PR) according to RECIST 1.1 criteria, including one patient who also achieved a complete metabolic response. One patient with cholangiocarcinoma was also considered to have achieved a PR by investigator assessment, demonstrating that gavo-cel has induced responses in every tumor type tested to date. The overall response rate (ORR) among patients who received gavo-cel following lymphodepletion chemotherapy was 22% by BICR and 26% by investigator assessment. By BICR, the ORR was 21% among patients with malignant pleural/peritoneal mesothelioma (MPM) and 29% among those with ovarian cancer. The median overall survival (OS) for patients with MPM was 11.2 months, whereas the median progression-free survival (PFS) for patients with MPM was 5.6 months.

The primary objectives of the Phase 1 portion of the trial are to evaluate the safety profile of gavo-cel in patients whose tumors overexpress mesothelin and to determine the RP2D. Secondary objectives include ORR and DCR. Exploratory objectives include the assessment of expansion, tumor infiltration and persistence of gavo-cel.

Summary of trial conduct, baseline characteristics and gavo-cel dose:

- **Screening:** Forty-eight percent of patients met the mesothelin expression cutoff as defined per protocol.
- **Patient Characteristics:** Thirty-two patients received gavo-cel including 23 with mesothelioma, eight with ovarian cancer and one with cholangiocarcinoma, with a median age of 63 years (range, 28-84 years). The median number of prior therapies was five (range 1-13), including immune checkpoint inhibitor therapy in 66% of patients and mesothelin directed therapy in 19% of patients.
- **gavo-cel Dose:** The 32 patients disclosed to date have received gavo-cel at the following DL:
 - **DL 0:** 5x10⁷ cells/m² without lymphodepletion – one mesothelioma
 - **DL 1:** 5x10⁷ cells/m² following lymphodepletion – seven mesothelioma and one ovarian cancer

- **DL 2:** 1×10^8 cells/m² without lymphodepletion – one mesothelioma
- **DL 3:** 1×10^8 cells/m² following lymphodepletion – six mesothelioma, one cholangiocarcinoma and six ovarian cancer
- **DL 3.5:** 3×10^8 cells/m² following lymphodepletion – four mesothelioma and one ovarian cancer
- **DL 4:** 5×10^8 cells/m² without lymphodepletion – one mesothelioma
- **DL 5:** 5×10^8 cells/m² following lymphodepletion – three mesothelioma

Key topline clinical findings from patients treated with gavo-cel:

- **Safety Data:** gavo-cel was generally well tolerated with a manageable adverse event profile up to DL5. Over the course of the Phase 1 clinical trial, two DLTs were observed: one case of Grade 3 pneumonitis at DL1 that resolved with anti-cytokine therapy, and one case of Grade 5 bronchialveolar hemorrhage at DL5. All three patients treated at DL5 experienced severe cytokine release syndrome (CRS) which resulted in the Safety Review Team recommending de-escalation. The most frequent Grade 3 or higher non-hematological toxicity among patients treated at the RP2D was CRS, which was reported in 15% of patients.
- **Clinical Activity:** Thirty patients were evaluable for response. DCR was 77%. Tumor regression was observed in 28 (93%) patients. Eight patients experienced target lesion regression greater than 30%, including six patients who achieved a PR by RECIST criteria (four with MPM and two with ovarian cancer). The ORR by RECIST criteria among patients infused with gavo-cel following lymphodepletion chemotherapy was 22% by BICR, which includes one patient who achieved a complete metabolic response, and 26% by investigator assessment, which includes an additional PR reported in a patient with metastatic cholangiocarcinoma.
- **Survival:** Among patients with mesothelioma, median OS and PFS were 11.2 months and 5.6 months, respectively, which compare favorably with the published outcomes of patients with relapsed refractory MPM treated in the second-line setting with standard therapy. Among patients with ovarian cancer, median OS and PFS were 8.1 months and 5.8 months, respectively.

Translational Data: Peak gavo-cel expansion (C_{max}) occurred between days 7 and 23. C_{max} markedly increased when gavo-cel was administered following lymphodepletion. Cytokine induction post gavo-cel infusion was observed in all evaluable patients, which is indicative of mesothelin target engagement. Post infusion, expression of PD-1 was observed to be upregulated on circulating gavo-cel T cells. Detection of gavo-cel in tumors and malignant effusions showed higher expansion and longer persistence in these tissues as compared to peripheral blood.

Corporate Presentation

The Company from time to time presents and/or distributes to the investment community slide presentations to provide updates and summaries of its business. On September 28, 2022, the Company hosted a conference call and webcast to discuss topline results from the Phase 1 portion of the gavo-cel Phase 1/2 clinical trial for mesothelin-expressing solid tumors. A copy of its “Gavo-cel Phase 1 Presentation” slide presentation is being filed herewith as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.2.

Statements contained under this Item 8.01, including Exhibit 99.2, regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to: including express or implied statements regarding the Company’s 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; the Company’s expectations for the safety and efficacy of, and enhancements to, gavo-cel, TC-510 and the Company’s other product candidates including compared to other T-cell therapy approaches; the Company’s expectations regarding the estimated patient populations and related market opportunities in gavo-cel’s, TC-510’s and the Company’s other product candidates’ targeted indications; the Company’s expectations regarding manufacturing of gavo-cel, TC-510 and the Company’s other product candidates, the Company’s expectations regarding its development programs and IND-enabling studies; the Company’s expectations regarding expansion opportunities for its TRuC platform; and the Company’s expectations regarding its financial position.

Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include, without limitation: 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 the Company's 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 the Company may be unable to gain approval of gavo-cel, TC-510 and the Company's other product candidates on a timely basis, if at all; the risk that the Company has over-estimated the potential patient population for its product candidates, if approved; the risk that the current COVID-19 pandemic will impact the Company's clinical trials and other operations; and other risks set forth under the caption "Risk Factors" in the Company's most recent Annual Report on Form 10-K, most recent Quarterly Report on Form 10-Q and its other filings with the Securities and Exchange Commission. All forward-looking statements contained in this presentation speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued by TCR2 Therapeutics Inc. on September 28, 2022.
99.2	Copy of TCR2 Therapeutics Inc. slide presentation dated September 28, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

TCR² THERAPEUTICS INC.

By: /s/ Eric Sullivan

Name: Eric Sullivan

Title: Chief Financial Officer

Date: September 28, 2022



**gavo-cel Continues to Demonstrate Clinical Benefit in Solid Tumors with
Additional RECIST Responses in Ovarian Cancer and Mesothelioma**

- Completed Phase 1 clinical trial establishes gavo-cel monotherapy as the first anti-mesothelin cell therapy to demonstrate tolerability and clinical benefit
 - Second RECIST partial response in ovarian cancer supports broad potential of gavo-cel
 - Consistent tumor regression in 28 of 30 (93%) evaluable patients with disease control rate of 77%
- Progression-free survival of 5.6 months and overall survival of 11.2 months suggest durability of benefit in mesothelioma
 - Phase 2 portion of trial underway implementing multiple approaches to further improve clinical outcomes
 - TCR² to host a conference call on Wednesday, September 28, 2022 at 8:00a.m. ET

CAMBRIDGE, Mass., September 28, 2022 – TCR² Therapeutics Inc. (Nasdaq: TCRR), a clinical-stage cell therapy company with a pipeline of novel T cell therapies for patients suffering from solid tumors, today announced positive topline results from the Phase 1 portion of the gavo-cel Phase 1/2 clinical trial for mesothelin-expressing solid tumors, with some patients still being monitored for clinical response or stable disease.

As of the September 9, 2022 data cutoff, 32 patients (including 23 mesothelioma, eight ovarian cancer and one cholangiocarcinoma) had received a single gavo-cel infusion in the Phase 1 portion of the clinical trial. The patients were heavily pretreated with a median of five prior lines of therapy, including immune checkpoint inhibitors in 66% of patients and mesothelin-directed therapies in 19% of patients. Following identification of a dose-limiting toxicity (DLT) at dose level (DL) 5 (5×10^8 cells/m² following lymphodepletion) in September 2021, the study proceeded to a dose de-escalation portion, first at DL3.5 (3×10^8 cells/m² following lymphodepletion) using a split-dosing approach, and subsequently at DL3 (1×10^8 cells/m² following lymphodepletion) which was declared the recommended Phase 2 dose (RP2D). No new DLTs were observed.

gavo-cel demonstrated a disease control rate (DCR) of 77%, which is defined in the Phase 1 portion of the trial as a response or sustained stable disease for at least 3 months post infusion. As measured by blinded independent central review (BICR), 28 of the 30 (93%) patients evaluable for efficacy experienced tumor regression of their target lesions, ranging in magnitude from 4% to 80%. Eight patients experienced target lesion regression greater than 30%, six of whom (four with mesothelioma and two with ovarian cancer) achieved a partial response (PR) according to RECIST 1.1 criteria, including one patient who also achieved a complete metabolic response. One patient with cholangiocarcinoma was also considered to have achieved a PR by investigator assessment, demonstrating that gavo-cel has induced responses in every tumor type tested to date. The overall response rate (ORR) among patients who received gavo-cel following lymphodepletion chemotherapy was 22% by BICR and 26% by investigator assessment. By BICR, the ORR was 21% among patients with malignant pleural/peritoneal mesothelioma (MPM) and 29% among those with ovarian cancer. The median overall survival (OS) for patients with MPM was 11.2 months, whereas the median progression-free survival (PFS) for patients with MPM was 5.6 months.

“We believe our Phase 1 clinical data already position gavo-cel as a first- and best-in-class anti-mesothelin monotherapy with a near-term opportunity during Phase 2 to further improve the depth and durability of clinical benefit by using it in combination with immune checkpoint inhibitors and redosing strategies. These are remarkable data in the context of solid tumors where there have been significant challenges with current CAR-T therapies. I am particularly excited by this second RECIST response in ovarian cancer as it supports the meaningful clinical activity of gavo-cel in a large patient population. Additionally, we continue to observe consistent tumor regression for heavily pre-treated patients with mesothelioma for whom limited options are available,” said Garry Menzel, Ph.D., President and Chief Executive Officer of TCR² Therapeutics. “As a result, we have narrowed our focus in the short-term to our three core programs, gavo-cel, TC-510 and TC-520, so that we can maximize the number of patients with access to our investigational therapies.”

“The results of the Phase 1 trial underscore the potential clinical value of gavo-cel in a very heavily pretreated patient population that are receiving our engineered T cells as their sixth line of therapy on average,” said Alfonso Quintás-Cardama, M.D., Chief Medical Officer of TCR² Therapeutics. “gavo-cel has demonstrated a manageable safety profile at the RP2D, induced RECIST responses in every indication studied to date, and has provided a promising survival signal among patients with mesothelioma as well as encouraging preliminary efficacy data in ovarian cancer. These results clearly support the further development of gavo-cel in the Phase 2 portion of the study where we believe that the combination with checkpoint inhibitors and the ability to retreat patients with additional doses of gavo-cel will allow us to increase patients’ exposure to gavo-cel, potentially translating into even higher response rates and improved durability of benefit.”

“We have already dosed a number of patients in combination with checkpoint inhibitors, including patients with ovarian cancer, in the randomized Phase 2 portion of the trial and look forward to providing ongoing progress updates on the various arms of the study as well as following the remaining patients still on the Phase 1 portion. We are clearly delighted that patients with various cancers continue to derive meaningful benefit from gavo-cel,” added Dr. Menzel.

The primary objectives of the Phase 1 portion of the trial are to evaluate the safety profile of gavo-cel in patients whose tumors overexpress mesothelin and to determine the RP2D. Secondary objectives include ORR and DCR. Exploratory objectives include the assessment of expansion, tumor infiltration and persistence of gavo-cel.

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Key topline clinical findings from patients treated with gavo-cel:

- **Safety Data:** gavo-cel was generally well tolerated with a manageable adverse event profile up to DL5. Over the course of the Phase 1 clinical trial, two DLTs were observed: one case of Grade 3 pneumonitis at DL1 that resolved with anti-cytokine therapy, and one case of Grade 5 bronchioalveolar hemorrhage at DL5. All three patients treated at DL5 experienced severe cytokine release syndrome (CRS) which resulted in the Safety Review Team recommending de-escalation. The most frequent Grade 3 or higher non-hematological toxicity among patients treated at the RP2D was CRS, which was reported in 15% of patients.
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- **Translational Data:** Peak gavo-cel expansion (C_{max}) occurred between days 7 and 23. C_{max} markedly increased when gavo-cel was administered following lymphodepletion. Cytokine induction post gavo-cel infusion was observed in all evaluable patients, which is indicative of mesothelin target engagement. Post infusion, expression of PD-1 was observed to be upregulated on circulating gavo-cel T cells. Detection of gavo-cel in tumors and malignant effusions showed higher expansion and longer persistence in these tissues as compared to peripheral blood.

About the Phase 1/2 Clinical Trial in Advanced Mesothelin-Expressing Solid Tumors

The Phase 1/2 clinical trial (NCT03907852) is evaluating the safety and efficacy of gavocabtagene autoleucel (“gavo-cel”; previously known as TC-210), TCR²’s T cell receptor fusion construct directed against mesothelin. The trial is enrolling patients with either mesothelin expressing non-small cell lung cancer (NSCLC), ovarian cancer, cholangiocarcinoma, or malignant pleural/peritoneal mesothelioma (MPM). The Phase 1 dose escalation portion of the clinical trial utilized a modified 3+3 design with four increasing gavo-cel doses. At each dose, gavo-cel was tested in two separate dose levels: first without lymphodepletion and then following lymphodepleting chemotherapy.

In the Phase 2 portion of the clinical trial, patients will receive gavo-cel at the recommended Phase 2 dose (1×10^8 cells/m² following lymphodepletion). A total of 75 patients will be treated in the MPM cohort and a total of 20 patients will be treated in each one of the following indications: ovarian, NSCLC and cholangiocarcinoma. In the MPM cohort, patients will be randomized to receive either single agent gavo-cel, gavo-cel in combination with OPDIVO® (nivolumab), or gavo-cel in combination with OPDIVO and YERVOY® (ipilimumab). Patients enrolled in the ovarian cancer, NSCLC or cholangiocarcinoma cohorts will all receive gavo-cel in combination with OPDIVO.

About Mesothelin-Expressing Solid Tumors

Mesothelin is a cell-surface glycoprotein highly expressed in a wide range of solid tumors, including malignant pleural/peritoneal mesothelioma, ovarian cancer, cholangiocarcinoma, breast cancer, pancreatic cancer and others. Overexpression of mesothelin is associated with poorer prognosis in some cancers due to its active role in both malignant transformation and tumor aggressiveness by promoting cancer cell proliferation, invasion, and metastasis. Of the wide range of solid tumors expressing mesothelin, non-small cell lung cancer, ovarian cancer, mesothelioma and cholangiocarcinoma represent a patient population up to 81,000 annually in the United States alone.

TCR² Therapeutics Conference Call and Webcast

TCR² Therapeutics will host a conference call and webcast on Wednesday, September 28, 2022 at 8:00am E.T. In order to participate in the conference call, please register at <https://bit.ly/3BTJ9Z7>. Participants can register via this link up to ten minutes prior to start time. The webcast and presentation will be made available on the TCR² Therapeutics website in the Investors section under Events at investors.tcr2.com/events. Following the live audio webcast, a replay will be available on the Company’s website for approximately 30 days.

About TCR² Therapeutics

TCR² Therapeutics Inc. is a clinical-stage cell therapy company developing a pipeline of novel T cell therapies for patients suffering from solid tumors. The Company is focused on the discovery and development of product candidates against novel and complex targets utilizing its proprietary T cell receptor (TCR) Fusion Construct T cells (TRuC®-T cells). The TRuC platform is designed to specifically recognize and kill cancer cells by harnessing signaling from the entire TCR, independent of human leukocyte antigens (HLA). For more information about TCR², please visit www.tcr2.com.

Forward-looking Statements

This press release contains forward-looking statements and information within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “will,” “could,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “seeks,” “endeavor,” “potential,” “continue” or the negative of such words or other similar expressions can be used to identify forward-looking statements. These forward-looking statements include, but are not limited to, express or implied statements regarding the therapeutic potential of gavo-cel, TC-510 and TCR²’s other product candidates, including

potential improvements in efficacy, safety and durability in the Phase 2 portion of the gavo-cel trial, expectations regarding future growth and prospects, future clinical development plans and anticipated timing of data updates, the development of the Company's TRuC-T cells, their potential characteristics, applications and clinical utility, and the potential therapeutic applications of the Company's TRuC-T cell platform.

The expressed or implied forward-looking statements included in this press release are only predictions and are subject to a number of risks, uncertainties and assumptions, including, without limitation: uncertainties inherent in clinical studies and in the availability and timing of data from ongoing clinical studies; whether interim and topline results from a clinical trial will be predictive of the final results of the trial; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future trials; the expected timing of submissions for regulatory approval or review by governmental authorities, including review under accelerated approval processes; orphan drug designation eligibility; regulatory approvals to conduct trials or to market products; TCR2's ability to maintain sufficient manufacturing capabilities to support its research, development and commercialization efforts, including TCR2's ability to secure additional manufacturing facilities; TCR2's ability to enroll patients in its clinical trials; whether TCR2's cash resources will be sufficient to fund TCR2's foreseeable and unforeseeable operating expenses and capital expenditure requirements, the impact of the COVID-19 pandemic on TCR2's ongoing operations; and other risks set forth under the caption "Risk Factors" in TCR2's most recent Annual Report on Form 10-K, most recent Quarterly Report on Form 10-Q and its other filings with the Securities and Exchange Commission. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this press release may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although TCR2 believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur.

Moreover, except as required by law, neither TCR2 nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements included in this press release. Any forward-looking statement included in this press release speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Investor and Media Contact:

Carl Mauch
Senior Director, Investor Relations and Corporate
Communications (617) 949-5667
carl.mauch@tcr2.com

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Phase 1 Dataset

September 2022

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.

Agenda

- **Phase 1 Key Takeaways** | Garry Menzel, PhD
- **Gavo-cel Phase 1 Data** | Alfonso Quintás-Cardama, MD
- **KOL: Gavo-cel Experience in the Clinic** | Raffit Hassan, MD
- **KOL: Standard of Care in Mesothelioma** | Patrick Forde, MD
- **Gavo-cel Phase 2 Trial Design** | Garry Menzel, PhD
- **Q&A**

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

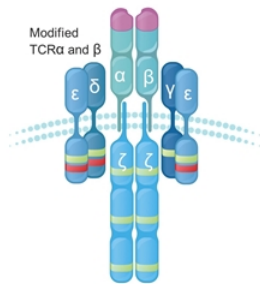
Baseline Established

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

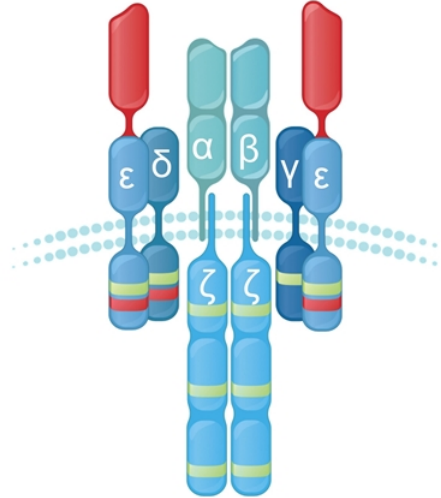
- ✓ Combination with checkpoint inhibitors
 - ✓ Redosing
 - ✓ Earlier lines of therapy

TRuCs Represent Advancement Upon Existing T Cell Therapies

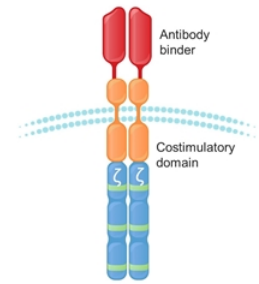
TCR-T Cell (T Cell Receptor)



TRuC-T Cell (T Cell Receptor Fusion Construct)



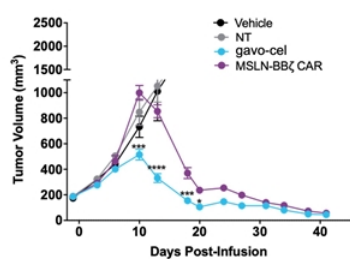
CAR-T Cell (Chimeric Antigen Receptor)



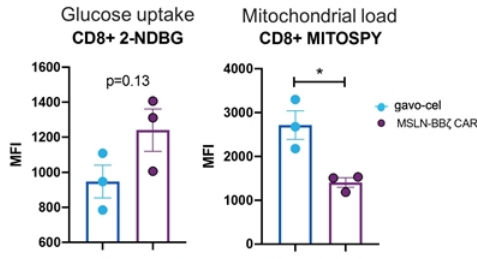
- ✓ Utilizes Full TCR Complex Signaling
- ✓ HLA Independent

Preclinically, TRuCs Show Superiority Over CARs

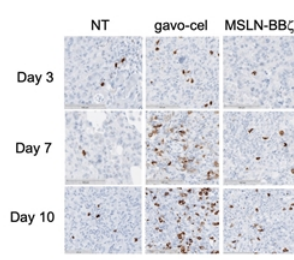
Superior Tumor Control vs. CAR-Ts



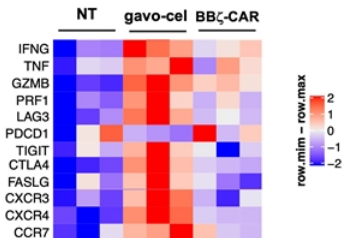
Optimal Metabolic Profile for Enhanced Fitness



Superior Intratumoral Infiltration



Higher Gene Expression Associated with T Cell Activation and Migration



Clinically, gavo-cel Has Shown Activity Where Others Have Failed

First Anti-Mesothelin Cell Therapy to Demonstrate Tolerability and Clinical Benefit



Memorial Sloan Kettering
Cancer Center



ATARA BIO®

74 Patients treated with anti-mesothelin
CAR-T monotherapy

1

Total RECIST Responses reported

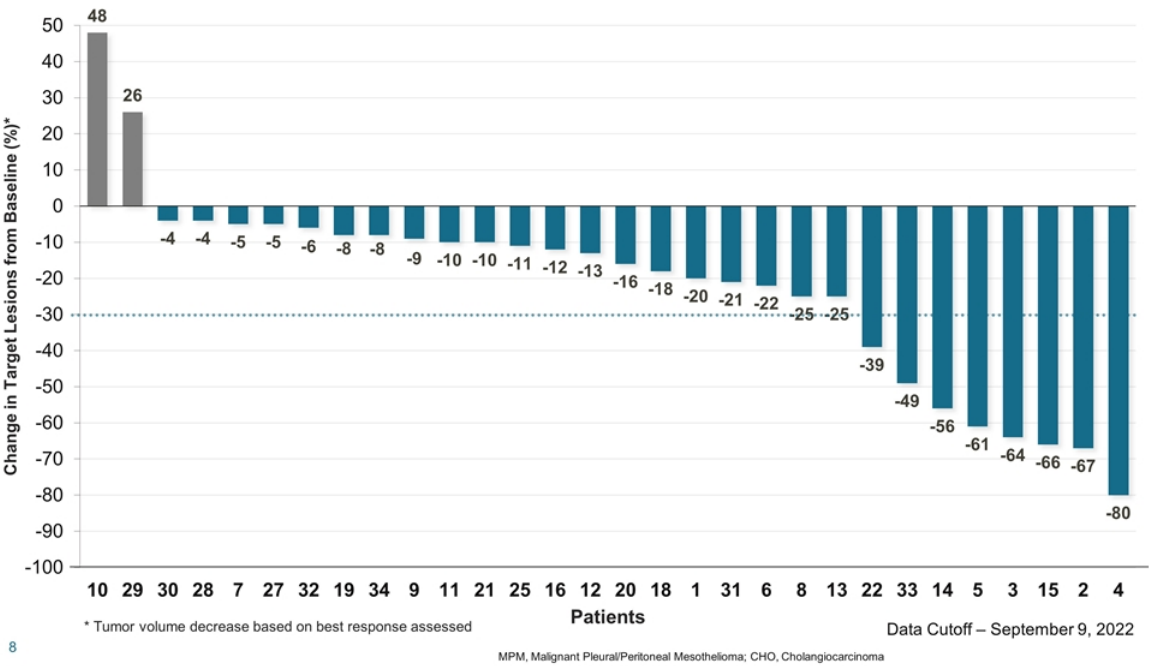


30 Patients evaluable treated with gavo-cel
(TRuC-T cell) monotherapy

6

Total RECIST Responses reported

gavo-cel Achieved Consistent Tumor Regression in 93% of Evaluable Patients



MPM

21/22

Ovarian

6/7

CHO

1/1

** CHO PR by Investigator Assessment



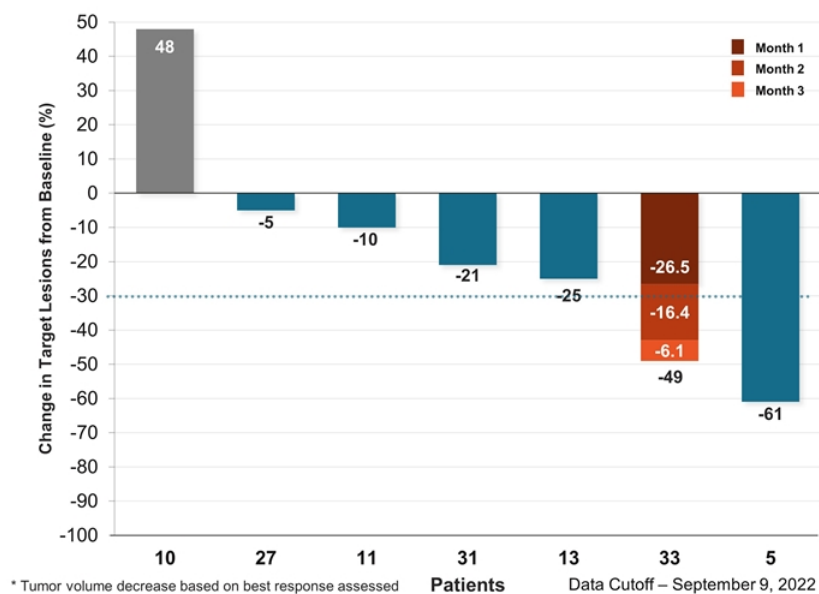
Promising Signal in Platinum Refractory Ovarian Cancer

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%)

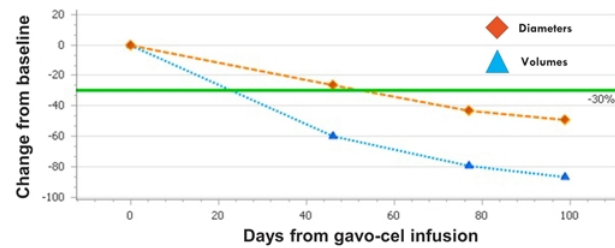
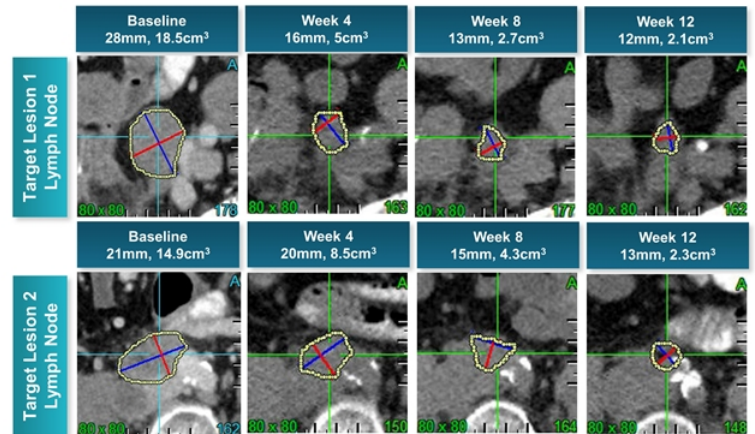
66-year-old female,

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 $1 \times 10^8/m^2$ (RP2D)



TCR²
THERAPEUTICS

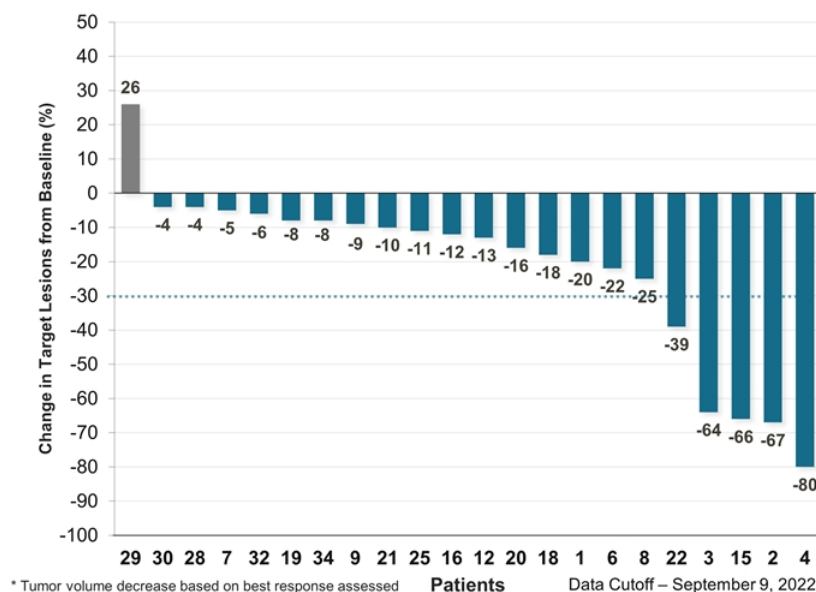
Phase 1 Data Support a Path Forward as Mesothelioma Leader

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

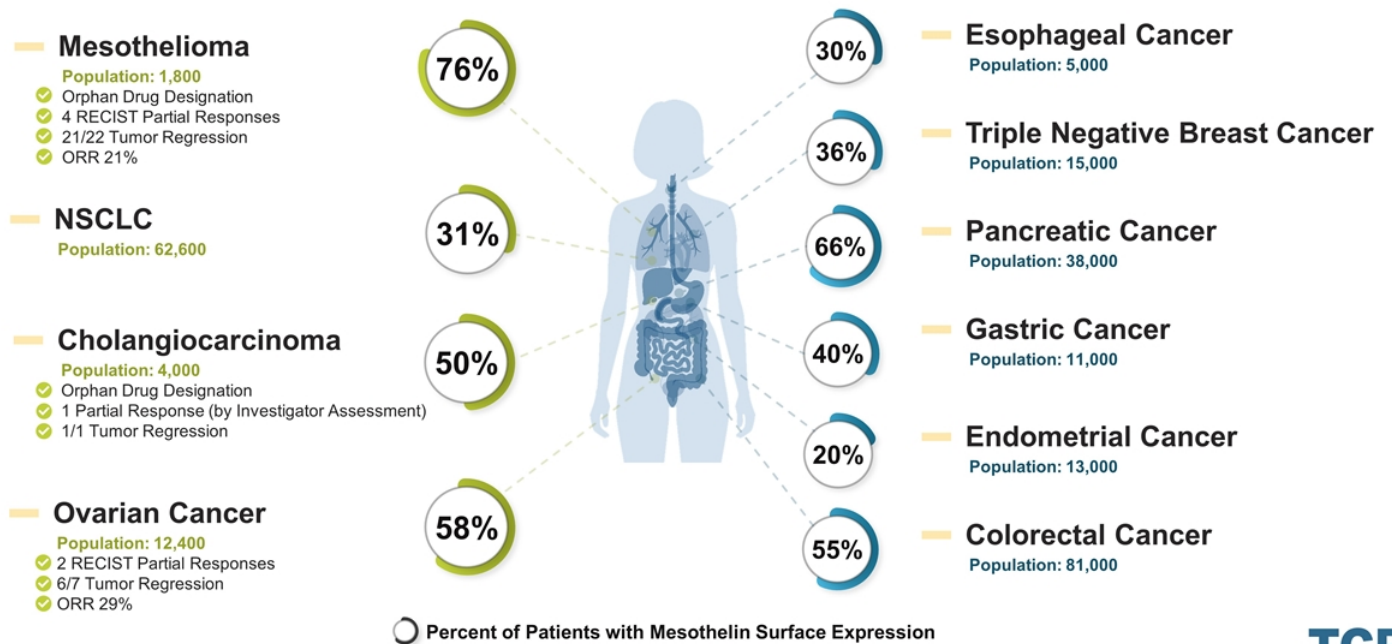
Efficacy Data

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



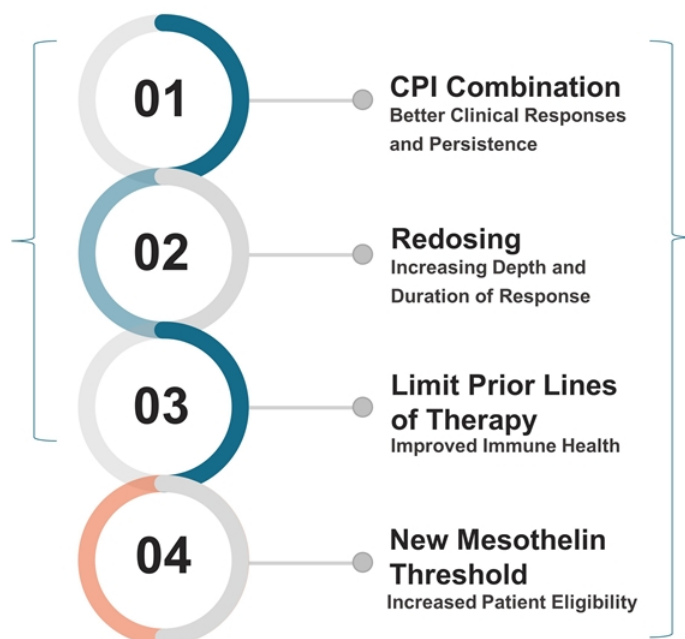
Significant Potential Opportunity in Mesothelin-Expressing Solid Tumors

~215,000 Patients Across Multiple Target Indications



Phase 2 Modifications Aim to Further Improve Outcomes and Patient Access

**Ovarian Cancer +
Mesothelioma**



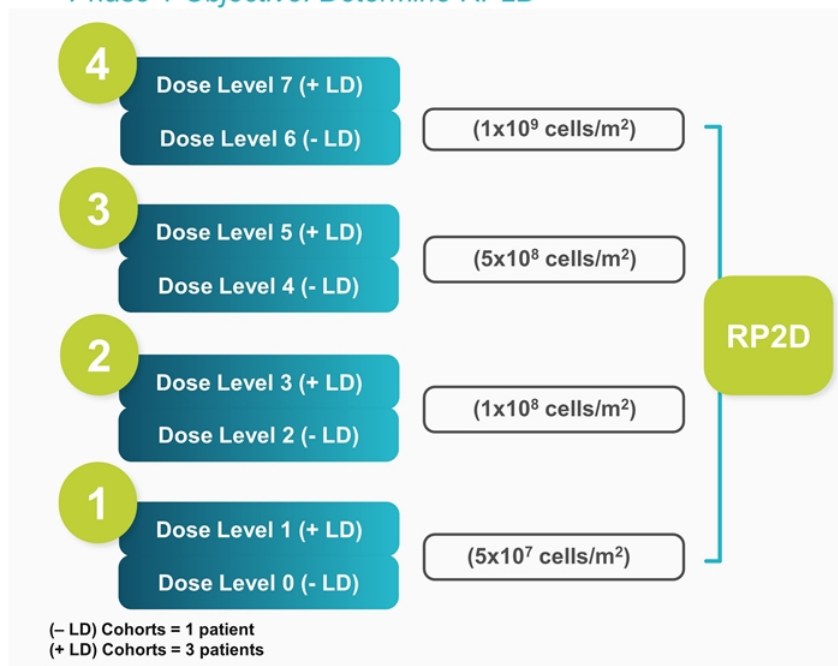
**NSCLC +
Cholangiocarcinoma**



Phase 1 Data

gavo-cel Phase 1 Trial in MSLN+ Solid Tumors

Phase 1 Objective: Determine RP2D



Phase 1: Dose Finding

Indications

- MPM
- Ovarian cancer
- NSCLC
- Cholangiocarcinoma

Mesothelin Expression

- IHC assay
- Central lab (Roche/Ventana)
- Cut-off: $\geq 50\%$ 2+/3+

Lymphodepletion (LD)

- Fludarabine: 30 mg/m² x4d
- Cyclophosphamide: 600 mg/m² x3d

Patient Tumor Characteristics

Dose Level (gavo-cel dose) No. Patients	RP2D							Overall n=32 (%)
	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	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	
Age, Median (Range)	61	70 (36-84)	46	59 (28-70)	63 (43-69)	67	52 (37-66)	63 (28-84)
Diagnosis	1 MPM	7 MPM 1 Ovarian	1 MPM	6 MPM, 6 Ovarian 1 Cholangio	4 MPM, 1 Ovarian	1 MPM	3 MPM	23 MPM 8 Ovarian 1 Cholangio
MSLN 2+/3+	90	72 (55-100)	90	70 (50-95)	75 (50-92)	60	65 (65-73)	70 (50-100)
Median No. Prior Rx	8	5	9	5	7	7	4	5 (1-13)
Prior ICI, n (%)	1 (100)	6 (75)	1 (100)	6 (46)	4 (80)	1 (100)	2 (66)	21 (66)
Prior Anti-MSLN Therapy, n (%)	1 (100)	1 (13)	1 (100)	1 (8)	2 (40)	0	1 (33)	6 (19)
Bridging Therapy, n (%)	0	6 (75)	0	12 (92)	5 (100)	1 (100)	1 (33)	25 (78)

Data Cutoff – September 9, 2022



Grade ≥3 Treatment Emergent Adverse Events

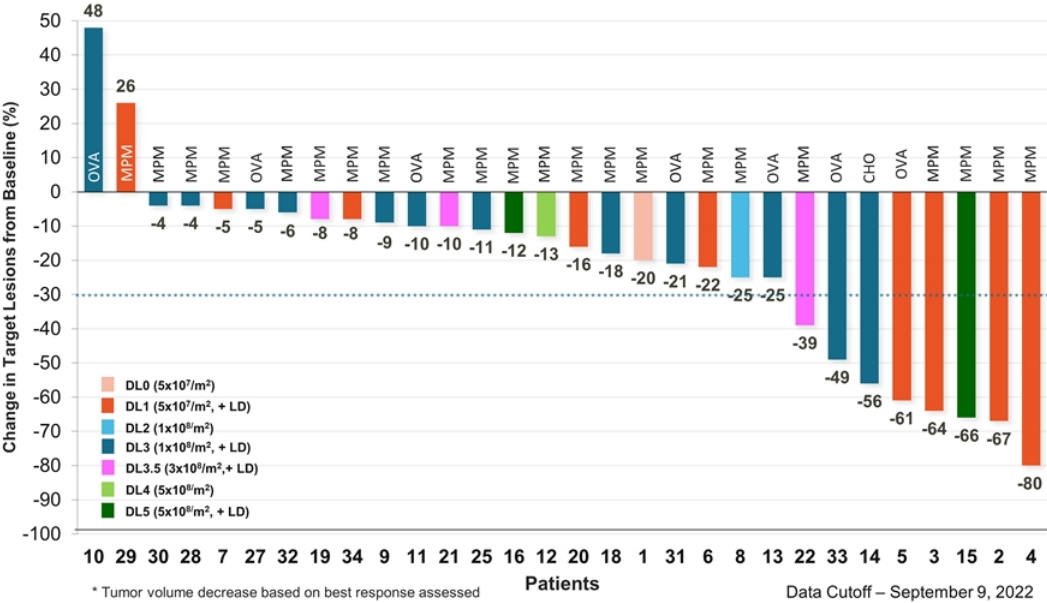
				RP2D				
Adverse Event	DL 0 (no LD) 5x10 ⁷ /m ² n=1 (%)	DL 1 5x10 ⁷ /m ² n=8 (%)	DL 2 (no LD) 1x10 ⁸ /m ² n=1 (%)	DL 3 1x10 ⁸ /m ² n=13 (%)	DL 3.5 3x10 ⁸ /m ² n=5	DL 4 (no LD) 5x10 ⁸ /m ² n=1 (%)	DL 5 5x10 ⁸ /m ² n=3 (%)	Overall n=32 (%)
Hematologic								
Lymphopenia	0	8 (100)	0	13 (100)	5 (100)	0	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

Consistent Tumor Regression in Patients with gavo-cel

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

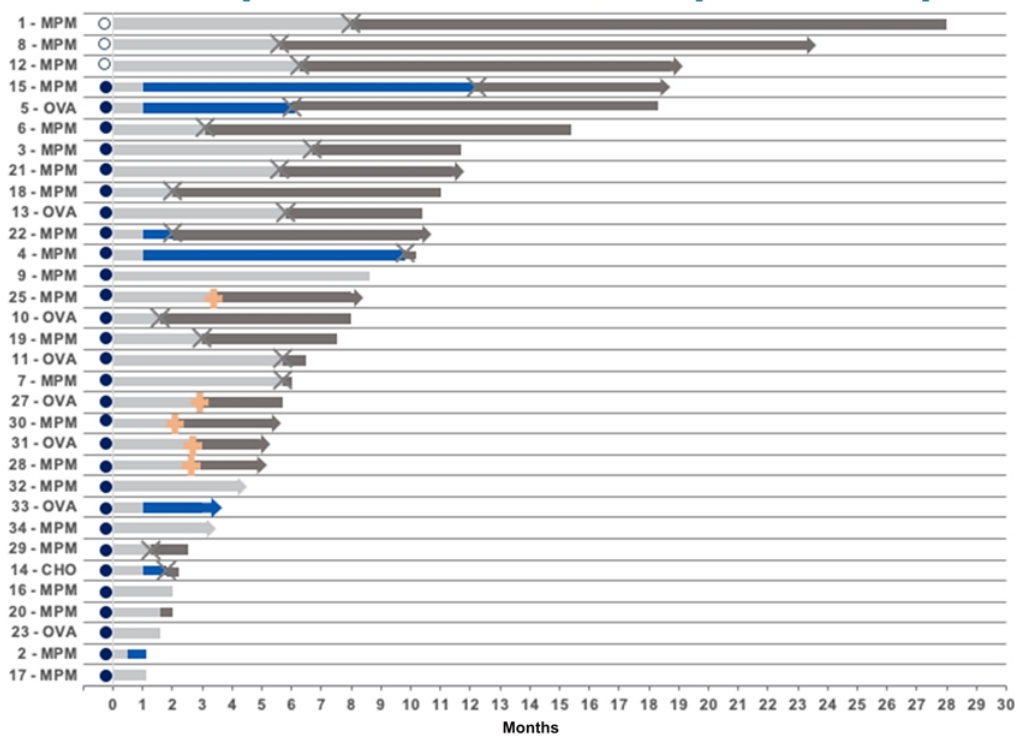


Blinded Independent Central Review

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

DCR = PR or SD lasting at least 3 months

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

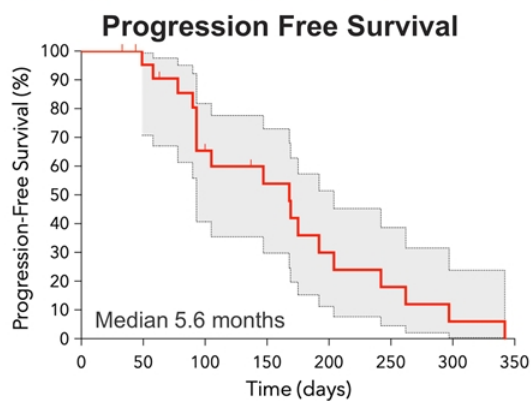
✚ Off Active FU (Unconfirmed PD)
(e.g. Clinical prog/inv. decision)

➡ Alive (ongoing) □ Deceased

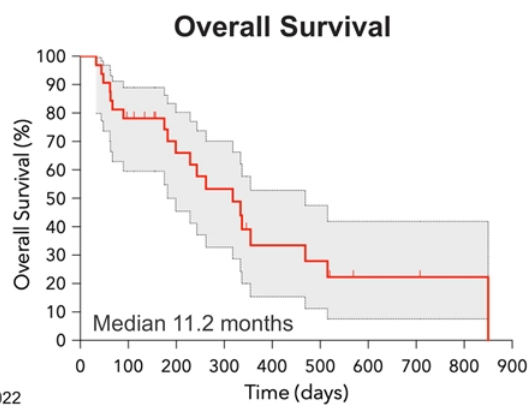
TCR²
THERAPEUTICS

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 vs Supportive Care ¹	98	3.1	4.2	9.3
	56	1.8	2.8	9.1
Pembrolizumab vs Vinorelbine or Gemcitabine ²	73	22	2.5	10.7
	71	6	3.4	12.4
Nivolumab vs Placebo ³	221	11	3	10.2
	111	1	1.8	6.9

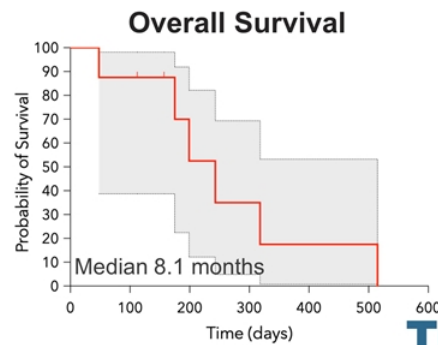
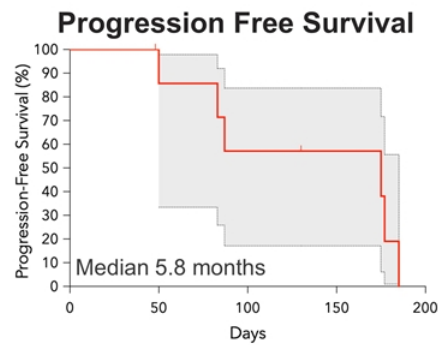
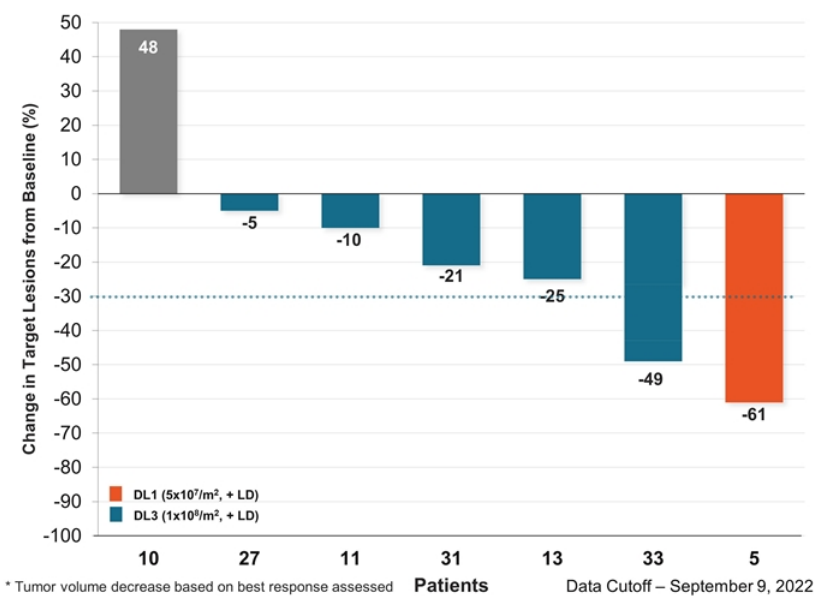
Benchmarks in Second Line Post Platinum-Based Therapy

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

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

Survival in Ovarian Cancer after gavo-cel Infusion

ORR 29%, PFS 5.8 Months, OS 8.1 Months



Patient 5 – Platinum Refractory Ovarian Cancer

Partial Response (RECIST v1.1), Tumor Regression (61%)

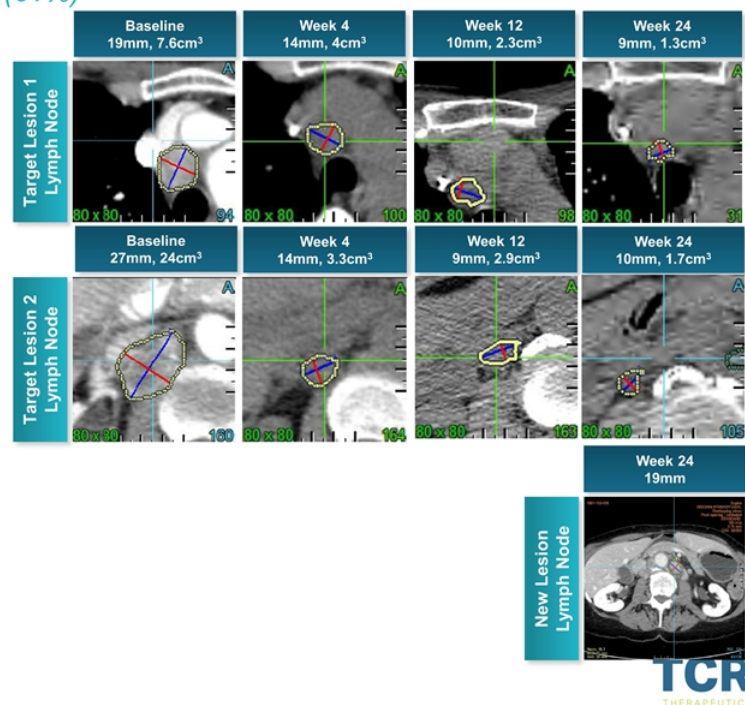
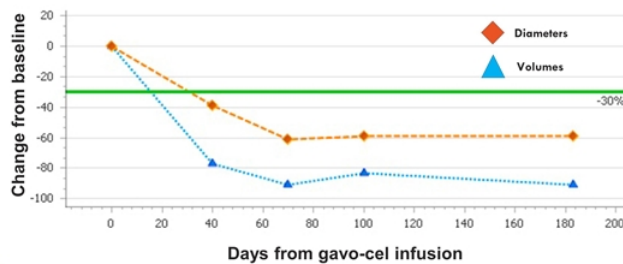
70-year-old female

High grade, Stage IV serous ovarian cancer

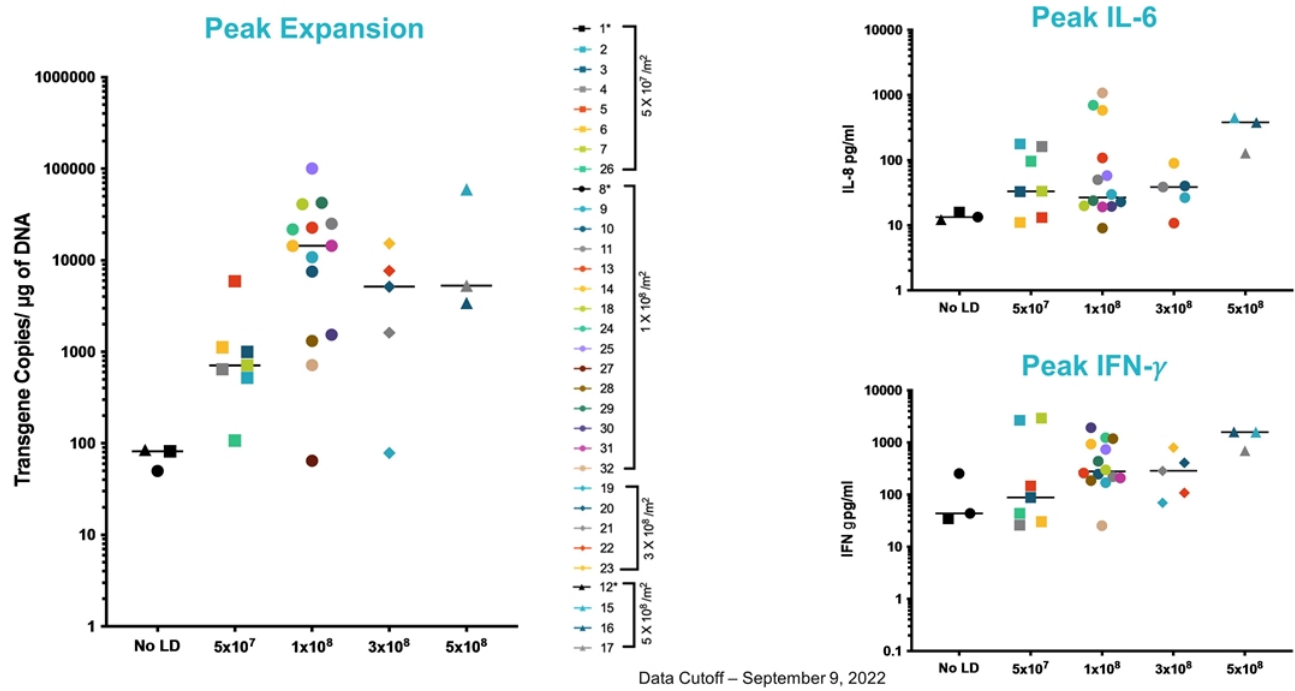
- *TP53*^{R248Q}, *CCNE1* amplified, wild type *BRCA1/2*
- Failed 6 prior lines of chemotherapy

Enrolled in gavo-cel Clinical Trial

- Lymphodepletion with Flu/Cy
- gavo-cel at $5 \times 10^7/m^2$ (Dose Level 1)

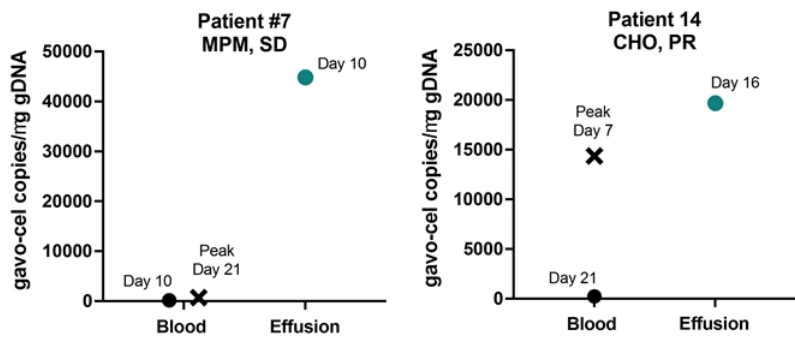


gavo-cel Displayed Dose-Dependent Expansion and Cytokine Release

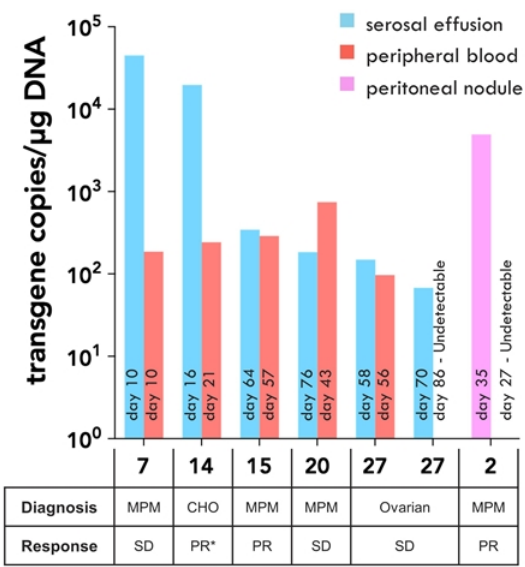


Intratumor Infiltration and Persistence Greater Than in Blood

TRuC-T Cell Migration and Infiltration Evident from Serous Effusions



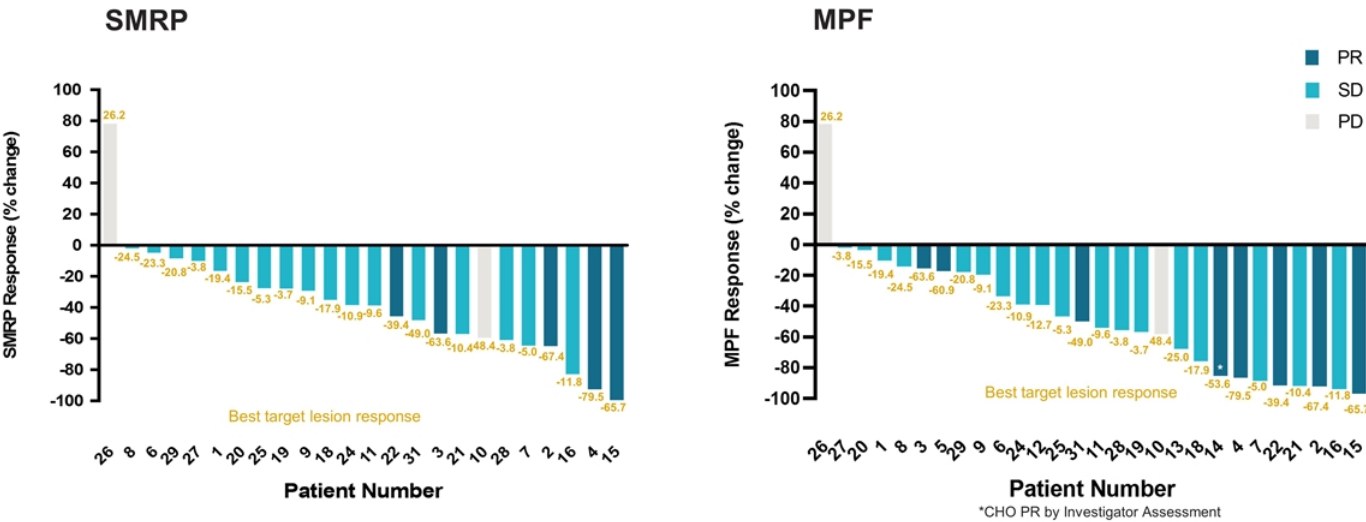
Analysis performed in a subset of patients (n=6); all analyzable samples showed detectable levels of gavo-cel, but not all showed increased expansion at disease sites



Data Cutoff – September 9, 2022 * PR by Investigator Assessment

Diagnosis	MPM	CHO	MPM	MPM	Ovarian	MPM
Response	SD	PR*	PR	SD	SD	PR

gavo-cel: SMRP and MPF Data vs. Best Target Lesion Response



Patients with baseline levels of SMRP in normal range were excluded

Data Cutoff – September 9, 2022

SMRP, Soluble Mesothelin-Related Peptides; MPF, Megakaryocyte Potentiating Factor; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease; CHO, Cholangiocarcinoma



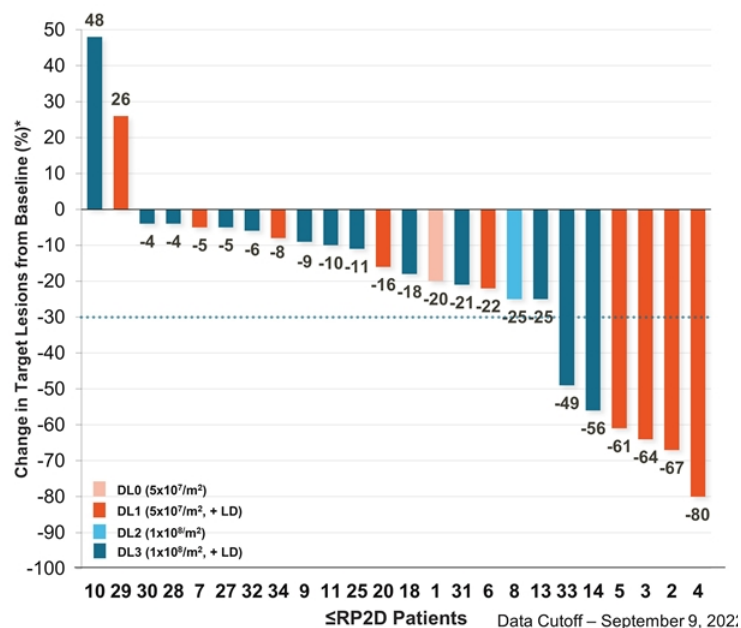


Phase 2 Trial

Trial Modifications & Design

Clinical Activity At or Below gavo-cel RP2D

- Manageable safety profile
- Clinical activity at \leq RP2D in 3/3 tumor indications
- 5 RECIST PRs
- Multiple patients near 30% tumor regression



* Tumor volume decrease based on best response assessed

DL, Dose Level; LD, Lymphodepletion; RP2D, Recommended Phase 2 Dose; PR, Partial Response

Phase 2 Incorporates Four Changes Aiming to Boost Patient Outcomes

Broadening Patient Access

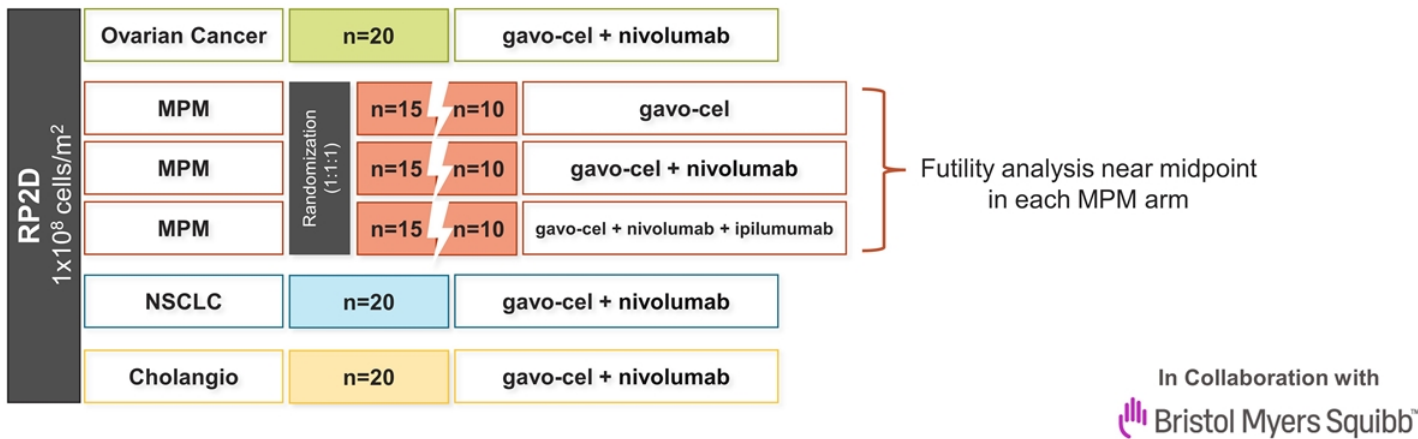
- 1 Increased Patient Eligibility with New MSLN Threshold for NSCLC and Cholangiocarcinoma

Durability and Persistence

- 2 Redosing (LD + gavo-cel)
- 3 Checkpoint Inhibitor Combinations
- 4 Limit Prior Lines of Therapy ≤ 5

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

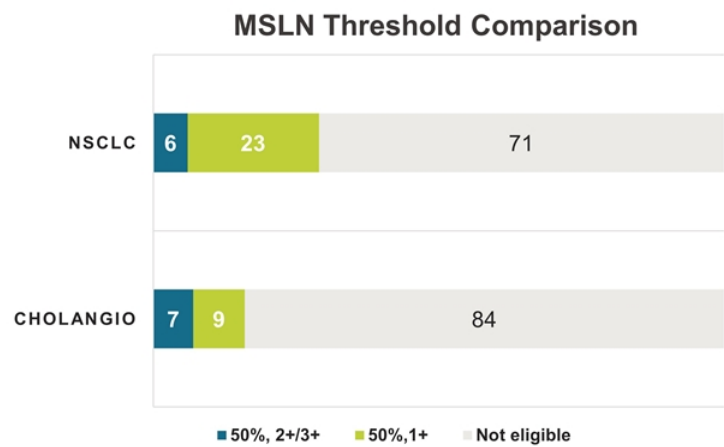
- Patient with a confirmed response (i.e. PR or CR) and then exhibits symptoms or signs of PD
- Patients with SD for at least 8 weeks

Increase in Patient Eligibility with New MSLN Threshold

New Threshold:
≥50% tumor cells irrespective of MSLN intensity (1+/2+/3+)

Non-Small Cell Lung Cancer
29% patients eligible for therapy based on Phase 2 threshold

Cholangiocarcinoma
16% patients eligible for therapy based on Phase 2 threshold



Data based on internal analysis in September 2022

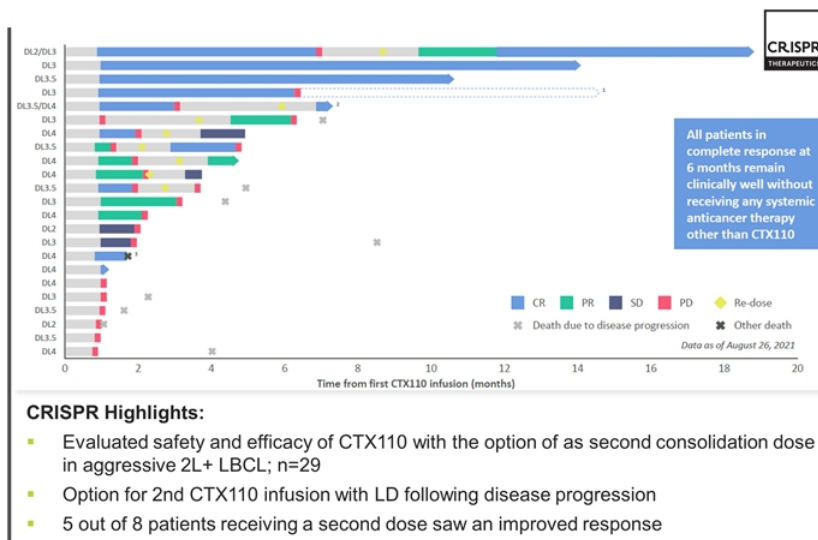
Redosing Allowed from 12 Weeks, Could Deepen Patient Responses

Based on gavo-cel Phase 1 manufacturing experience:

100% Patients had 2 doses from one manufacturing run

97% Patients had 3 doses from one manufacturing run

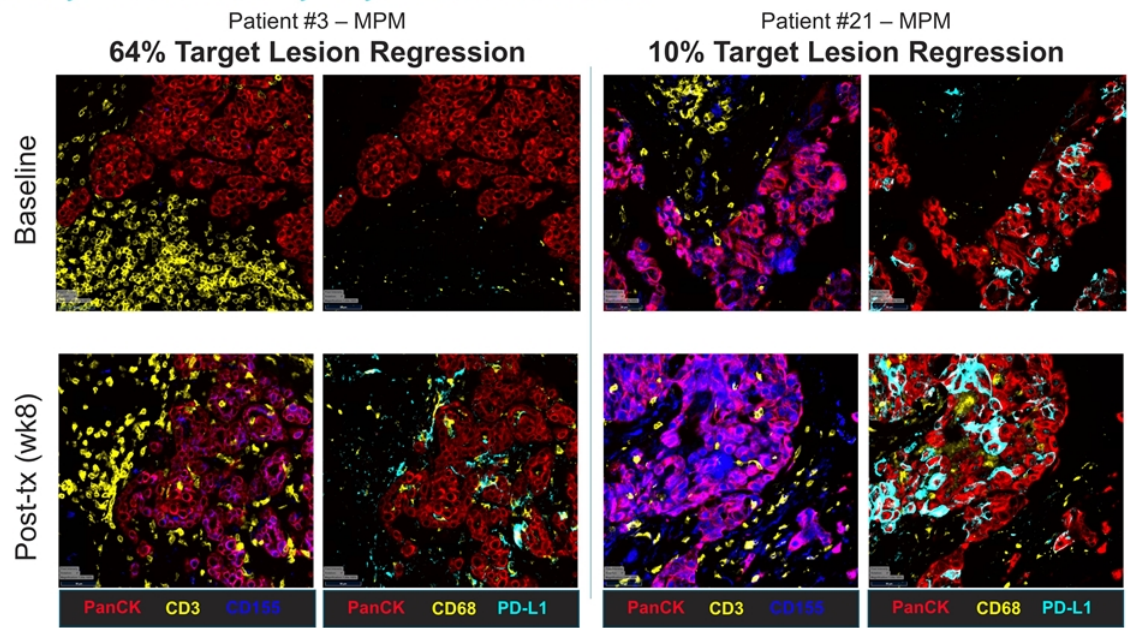
46% Patients eligible for a redosing based on Phase 2 protocols



Source: CRISPR public materials, Trial: [NCT04035434](https://clinicaltrials.gov/ct2/show/study/NCT04035434) (CARBON)

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

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
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						

Q&A