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 17, 2021

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

Delaware	**001-38811**	**47-4152751**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(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 17, 2021, TCR2 Therapeutics Inc. (the "Company") issued a press release titled "TCR2 Therapeutics Announces Positive Interim Results from Ongoing Phase 1/2 Trial of Gavo-cel for Treatment Refractory Mesothelin-Expressing Solid Tumors." 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.

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 17, 2021, the Company hosted a conference call and webcast to discuss interim data from the ongoing Phase 1 portion of the gavo-cel Phase 1/2 clinical trial for mesothelin-expressing solid tumors. A copy of its "Gavo-cel Phase 1/2 Clinical Update" 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: express or implied statements regarding TCR2's expectations for the Phase 1/2 clinical trials of gavo-cel and TC-110; TCR2's expectations for the safety and efficacy of its product candidates and enhancements, including gavo-cel and TC-110, compared to current T-cell therapy approaches; TCR2's expectations regarding the timing of determining an RP2D for gavo-cel; TCR2's expectations regarding the estimated patient populations and related market opportunities in gavo-cel's and TC-110's targeted indications; and TCR2's expectations regarding manufacturing of its product candidates.

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 TCR2's planned clinical trials, including the Phase 1/2 clinical trials of gavo-cel and TC-110; the risk that the results from the Phase 1/2 clinical trials of gavo-cel and TC-110 will not support further development and marketing approval; the risk that TCR2 may be unable to gain approval of gavo-cel, TC-110 and its other product candidates on a timely basis, if at all; the risk that TCR2 has over-estimated the potential patient population for its product candidates, if approved; the risk that the current COVID-19 pandemic will impact TCR2's clinical trials and other 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. 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 17, 2021.
99.2	Copy of TCR2 Therapeutics Inc. slide presentation dated September 17, 2021.
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/ Mayur (Ian) Somaiya
Name: Mayur (Ian) Somaiya
Title: Chief Financial Officer

Date: September 17, 2021

TCR2 Therapeutics Announces Positive Interim Results from Ongoing Phase 1/2 Trial of Gavo-cel for Treatment Refractory Mesothelin-Expressing Solid Tumors

- Clinical activity observed in all three mesothelin-expressing tumor types treated
- Gavo-cel disease control rate (DCR) 81% with tumor regression in 15 of 16 evaluable patients
- Overall response rate (ORR) 31% in patients infused with gavo-cel following lymphodepletion
- Meaningful survival benefit at 11.2 months for patients with refractory mesothelioma
- Recommended Phase 2 Dose (RP2D) being refined after identification of the Maximum Tolerated Dose (MTD)
- TCR2 to host a conference call on Friday, September 17 at 9:00a.m. ET

CAMBRIDGE, Mass., Sept. 17, 2021 - TCR2 Therapeutics Inc. (Nasdaq: TCRR), a clinical-stage cell therapy company with a pipeline of novel T cell therapies for patients suffering from cancer, today announced positive interim results from the ongoing Phase 1 portion of the gavo-cel Phase 1/2 clinical trial for mesothelin-expressing solid tumors. A dataset will also be featured in an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2021 on September 17 at 14:20 CEST (8:20am EST) (Presentation #959O) and is part of the official ESMO Press Programme.

As of the June 30, 2021 data cutoff, 17 patients (12 mesothelioma, 4 ovarian cancer and 1 cholangiocarcinoma) had received a single gavo-cel infusion in the dose escalation portion of the gavo-cel Phase 1 clinical trial. The median number of prior lines of therapy was 5, including immune checkpoint inhibitors (n=11) and mesothelin-directed therapies (n=5). Gavo-cel was administered up to dose level 5 (DL5) ($5x10^8/m^2$ following lymphodepletion). Two dose limiting toxicities were reported: one Grade 3 pneumonitis at DL1 that resolved with supportive measures, which permitted the continuation of dose escalation, and one Grade 5 bronchoalveolar hemorrhage at DL5, which along with the development of severe CRS in all 3 patients treated at this dose level, led the Safety Review Team to declare $5x10^8/m^2$ as the MTD. Following identification of the MTD, one patient has received gavo-cel at $3x10^8/m^2$ after lymphodepletion using a split dosing approach to refine the RP2D and an additional patient has been treated at DL3 ($1x10^8/m^2$ following lymphodepletion). In both cases gavo-cel was well tolerated with only Grade 1 non-hematological toxicities being reported.

15 of the 16 patients evaluable for efficacy experienced regression of their target lesions, ranging in magnitude from 5% to 75%. Six patients achieved partial responses (PRs) by target lesion assessment, four of whom (3 with mesothelioma and 1 with ovarian cancer) achieved a PR according to RECIST 1.1 criteria, including one who also achieved a complete metabolic response. One patient with cholangiocarcinoma was also considered to have achieved a PR by investigator assessment, for an ORR of 31%. By independent review assessment, the ORR was 25% with a DCR Rate of 81%. The median overall survival for patients with mesothelioma is 11.2 months, whereas the median progression free survival is 5.9 months.

“The interim gavo-cel data reported today showed continued clinical benefit and a manageable safety profile in a population of patients that previously achieved minimal or no improvement due to the advanced and aggressive state of their cancer,” said principal investigator David Hong, M.D., deputy chair of the Department of Investigational Cancer Therapeutics at The University of Texas MD Anderson Cancer Center. “Patients with treatment refractory cancer have very limited treatment options and will often need hospice and supportive care. We are encouraged by the early survival data from gavo-cel in patients previously treated with checkpoint inhibitors and other therapies.”

“Our ambition with gavo-cel from the start was to redefine treatment for solid tumors with cell therapies. We are excited to present data demonstrating clinical activity in all three mesothelin-expressing solid tumors treated to date and tumor regression in a majority of patients who are treatment refractory after numerous lines of therapy. We are very encouraged by the progression free survival and overall survival observed among patients with refractory mesothelioma treated so far with gavo-cel in the Phase 1 trial,” said Alfonso Quintás-Cardama, M.D., Chief Medical Officer of TCR2 Therapeutics. “Based on these data and the most recent patient experiencing a very mild safety profile at a cell dose of $3x10^8/m^2$, we believe the identification of the RP2D is close at hand. As we approach the Phase 2 expansion phase, our focus will shift to further optimizing outcomes for patients by studying combinations with immune checkpoint inhibitors, allowing gavo-cel re-treatment and evaluating different mesothelin expression thresholds.”

The primary objectives of the Phase 1 portion of the trial are to define 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-six percent of patients met the mesothelin expression cut-off as defined per protocol.
- **Patient Characteristics**: 17 patients received gavo-cel including 12 with mesothelioma, 4 with ovarian cancer and 1 with cholangiocarcinoma with a median age of 57 years (range, 31-84 years). The median number of prior therapies was 5 (range, 1-9), including immune checkpoint inhibitor therapy (n=11) and anti-mesothelin therapies (n=5).
- **Gavo-cel Dose**: The seventeen patients disclosed to date have received gavo-cel at the following dose level (DL):
  - **DL 0:** $5x10^7$ cells/m^2 without lymphodepletion – 1 mesothelioma patient
  - **DL 1:** $5x10^7$ cells/m^2 following lymphodepletion – 5 mesothelioma patients and 1 ovarian cancer patient
  - **DL 2:** $1x10^8$ cells/m^2 without lymphodepletion – 1 mesothelioma patient
  - **DL 3:** $1x10^8$ cells/m^2 following lymphodepletion – 1 mesothelioma patient, 1 cholangiocarcinoma patient, and 3 ovarian cancer patients
  - **DL 4:** $5x10^8$ cells/m^2 without lymphodepletion – 1 mesothelioma patient
  - **DL 5:** $5x10^8$ cells/m^2 following lymphodepletion – 3 mesothelioma patients

Key clinical findings from patients treated with gavo-cel:

- **Safety**: gavo-cel was generally well tolerated with a manageable adverse event profile with no patients experiencing on-target, off-tumor toxicities. Two DLTs were observed: one case of Grade 3 pneumonitis at DL1 that resolved with anti-cytokine therapy, and one case of Grade 5 bronchoalveolar hemorrhage at DL5. Furthermore, all three patients treated at DL5 experienced Grade $\geq$3 CRS which resulted in $5x10^8$ cells/m^2 following lymphodepletion being declared the MTD.
- **Clinical Activity**: 16 patients were evaluable for response. Tumor regression was observed in 15 (94%) patients with a DCR of 81%. Six patients achieved partial responses (PRs) by target lesion assessment, four of whom (3 with mesothelioma and 1 with ovarian cancer) achieved a PR according to RECIST 1.1 criteria. The ORR by RECISTv1.1 criteria among patients infused with gavo-cel following lymphodepletion chemotherapy was 31% by independent review assessment, including one patient who achieved a complete metabolic response, and 38% by investigator assessment, which included a PR in a patient with metastatic cholangiocarcinoma.

- **Translational Data**: Peak gavo-cel expansion (C_{max}) increased when gavo-cel was administered following lymphodepletion in a dose dependent fashion. Cytokine elevations post-gavo-cel infusion were observed in all evaluable patients, which is indicative of mesothelin target engagement.

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"; TC-210), TCR^2'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. The Phase 1 dose escalation portion of the clinical trial utilizes a modified 3+3 design with four increasing gavo-cel doses. At each dose, gavo-cel will be tested in two separate dose levels: first without lymphodepletion and then following lymphodepleting chemotherapy. The Phase 1 portion of the clinical trial is ongoing.

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 80,000 annually in the United States alone.

TCR^2 Therapeutics Conference Call and Webcast

TCR^2 Therapeutics will host a conference call and webcast on Friday, September 17 at 9:00am E.T. In order to participate in the conference call, please dial 866-220-8062 (domestic) or 470-495-9169 (international) and refer to confirmation number 1597681. The webcast and presentation will be made available on the TCR^2 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 TCR^2 Therapeutics

TCR^2 Therapeutics Inc. is a clinical-stage cell therapy company developing a pipeline of novel T cell therapies for patients suffering from cancer. TCR^2's proprietary T cell receptor (TCR) Fusion Construct T cells (TRuC®-T cells) specifically recognize and kill cancer cells by harnessing signaling from the entire TCR, independent of human leukocyte antigens (HLA). In preclinical studies, TRuC-T cells have demonstrated superior anti-tumor activity compared to chimeric antigen receptor T cells (CAR-T cells), while secreting lower levels of cytokine release. The Company's lead TRuC-T cell product candidate targeting solid tumors, gavo-cel, is currently being studied in a Phase 1/2 clinical trial to treat patients with mesothelin-positive non-small cell lung cancer (NSCLC), ovarian cancer, malignant pleural/peritoneal mesothelioma, and cholangiocarcinoma. The Company's lead TRuC-T cell product candidate targeting hematological malignancies, TC-110, is currently being studied in a Phase 1/2 clinical trial to treat patients with CD19-positive adult acute lymphoblastic leukemia (aALL) and with aggressive or indolent non-Hodgkin lymphoma (NHL). For more information about TCR^2, 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 TCR2’s expectations for the Phase 1/2 clinical trials of gavo-cel and TC-110; TCR2’s expectations for the safety and efficacy of its product candidates and enhancements, including gavo-cel and TC-110, compared to current T-cell therapy approaches; TCR2’s expectations regarding the timing of determining an RP2D for gavo-cel and TCR2’s expectations regarding the estimated patient populations and related market opportunities in gavo-cel’s and TC-110’s targeted indications.

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 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 TCR2’s planned clinical trials, including the Phase 1/2 clinical trials of gavo-cel and TC-110; the risk that the results from the Phase 1/2 clinical trials of gavo-cel and TC-110 will not support further development and marketing approval; the risk that TCR2may be unable to gain approval of gavo-cel, TC-110 and its other product candidates on a timely basis, if at all; the risk that TCR2 has over-estimated the potential patient population for its product candidates, if approved; the risk that the current COVID-19 pandemic will impact TCR2’s clinical trials and other 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
Director, Investor Relations and Corporate Communications
TCR2 Therapeutics Inc.
(617) 949-5667
carl.mauch@tcr2.com

Exhibit 99.

TCR² THERAPEUTICS

POWERING THE TCR

TO TRANSFORM THE LIVES OF CANCER PATIENTS WITH SOLID TUMORS

gavo-cel Phase 1/2 Clinical Update

September 2021

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 trials of gavo-cel and TC-110, our expectations for the safety and efficacy of our product candidates and enhancements, including gavo-cel and TC-110, compared to current T-cell therapy approaches, our expectations regarding the timing of determining an RP2D for gavo-cel, our expectations regarding the estimated patient populations and related market opportunities in gavo-cel's and TC-110's targeted indications, and our expectations regarding manufacturing of our product candidates 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 trials of gavo-cel and TC-110; the risk that the results from the Phase 1/2 clinical trials of gavo-cel and TC-110 will not support further development and marketing approval; the risk that we may be unable to gain approval of gavo-cel, TC-110 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, 2020, as filed with the SEC on March 16, 2021, 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.

Introduction

Garry Menzel, PhD

Chief Executive Officer

Key Takeaways from gavo-cel Phase 1 Trial

3/3 Clinical Activity in All Tumor Types Treated

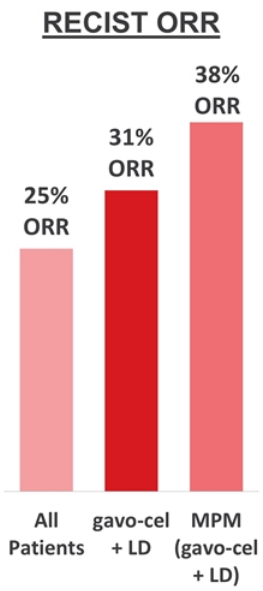
6 Partial Responses by Target Lesion Assessment

4 RECIST PRs in MPM (3) & Ovarian Cancer (1)

81% Disease Control Rate (DCR)

5.9 Median PFS (months) for MPM Patients

11.2 Median OS (months) for MPM Patients



MTD Identified at $5x10^8/m^2$ + LD

Approaching RP2D

Orphan Drug Designation for Mesothelioma and Cholangiocarcinoma

46% Patients Eligible for gavo-cel Based on Mesothelin Threshold

LD, Lymphodepletion; PR, Partial Response; ORR, Overall Response Rate; MTD, maximum tolerated dose; ODD, orphan drug designation; MPM, CCA

gavo-cel Clinical Trial Review

Alfonso Quintás-Cardama, MD
Chief Medical Officer

Ongoing gavo-cel Phase 1 Trial in MSLN+ Solid Tumors

Phase 1 Objective: Determine RP2D

Phase 1: Dose Finding

Indications

- Malignant mesothelioma
- Ovarian cancer
- Non-small cell lung cancer
- Cholangiocarcinoma

Mesothelin Expression

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

Lymphodepletion

- Fludarabine: 30 mg/m^2 x4d
- Cyclophosphamide: 600 mg/m^2 x3d

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

Patient Tumor Characteristics

Dose Level (gavo-cel dose) No. Patients	DL 0 (no LD) $5x10^7/m^2$ n=1	DL 1 $5x10^7/m^2$ n=6	DL 2 (no LD) $1x10^8/m^2$ n=1	DL 3 $1x10^8/m^2$ n=5	DL 4 (no LD) $5x10^8/m^2$ n=1	DL 5 $5x10^8/m^2$ n=3	Overall n=17 (%)
Age, median (range)	61	69 (36-84)	46	46 (31-63)	67	52 (37-66)	57 (31-84)
Diagnosis	1 MPM	5 MPM 1 Ovarian	1 MPM	1 MPM, 3 Ovarian 1 Cholangio	1 MPM	3 MPM	12 MPM 4 Ovarian 1 Cholangio
MSLN 2+/3+	90	81 (55-100)	90	60 (50-90)	60	65 (65-73)	73 (50-100)
Median No. Prior Rx	8	4	9	6	7	4	5 (1-9)
Prior ICI, n (%)	1 (100)	4 (67)	1 (100)	2 (40)	1 (100)	2 (66)	11 (65)
Prior anti-MSLN therapy, n (%)	1 (100)	1 (17)	1 (100)	1 (20)	0	1 (33)	5 (29)
Bridging Therapy, n (%)	0	4 (67)	0	4 (80)	1 (100)	1 (33)	10 (59)

Data Cutoff – June 30, 2021

MSLN, mesothelin; ICI, immune checkpoint inhibitor; MPM, malignant pleural/peritoneal mesothelioma; Cholangio, cholangiocarcinoma

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=6 (%)	DL 2 (no LD) $1x10^8/m^2$ n=1 (%)	DL 3 $1x10^8/m^2$ n=5 (%)	DL 4 (no LD) $5x10^8/m^2$ n=1 (%)	DL 5 $5x10^8/m^2$ n=3 (%)	Overall n=17 (%)
Hematologic							
Lymphopenia	1 (100)	6 (100)	0	5 (100)	1 (100)	3 (100)	16 (94)
Neutropenia	0	6 (100)	0	5 (100)	0	3 (100)	14 (82)
Thrombocytopenia	0	2 (33)	0	1 (20)	0	2 (67)	5 (29)
On Target / On Tumor							
CRS	0	2 (33)	0	1 (20)	0	3 (100)	6 (35)
Neurotoxicity	0	0	0	0	0	0	0
On Target / Off Tumor							
Pericarditis / Pericardial effusion	0	0	0	0	0	0	0
Pleuritis / Pleural effusion	0	0	0	0	0	0	0
Peritonitis/Ascites	0	0	0	0	0	0	0
Other							
Pneumonitis	0	1 (17)*	0	0	0	0	1 (6)
Sepsis	0	1 (17)	0	0	0	0	1 (6)
Hemorrhage	0	0	0	0	0	1 (33)*	1 (6)

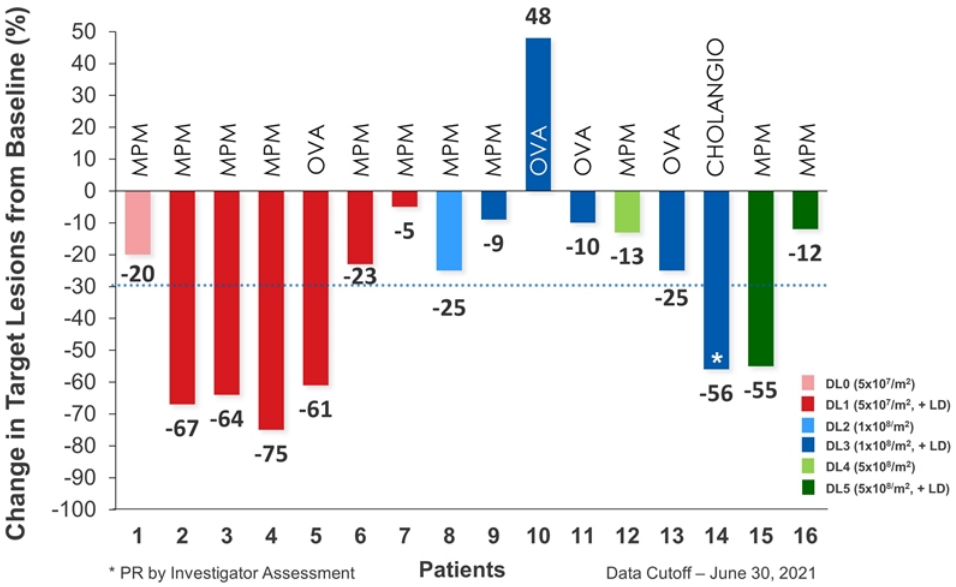
* Dose Limiting Toxicity

Data Cutoff – June 30, 2021

TCR² THERAPEUTICS

Consistent Tumor Regression in Patients with gavo-cel

Overall Response Rate 25%, Disease Control Rate 81%



* PR by Investigator Assessment

Data Cutoff – June 30, 2021

	All	gavo-cel + LD
DCR	81%	77%
ORR (independent)	25%	31%
ORR (investigator)	31%	38%
MPM ORR	27%	38%

DCR = PR or SD lasting at least 3 months

MPM, malignant pleural/peritoneal mesothelioma; OVA, ovarian cancer; CHOLANGIO, cholangiocarcinoma; DL, dose level; LD, lymphodepletion; DCR, disease control rate; ORR, overall response rate

Case Study: Patient 14 - Cholangiocarcinoma

Tumor Regression (56%)*

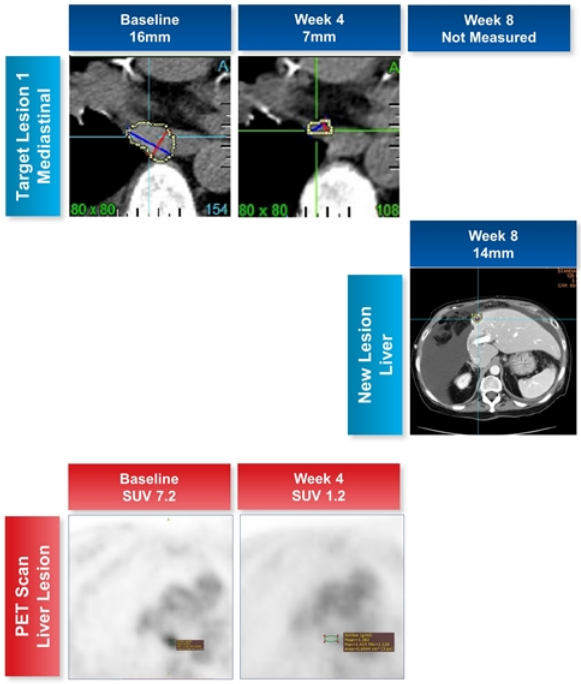
63-year-old female,

Metastatic intrahepatic cholangiocarcinoma

- Mutated *KRAS* and *RB1*
- Failed to respond to 5 prior lines of therapy

Enrolled in gavo-cel Clinical Trial Study

- **March 2021**: Lymphodepletion with Flu/Cy followed by gavo-cel at $1x10^8/m^2$



* PR by Investigator Assessment

Case Study: Patient 15 - Mesothelioma

Partial Response (RECIST v1.1), Tumor Regression (55%)

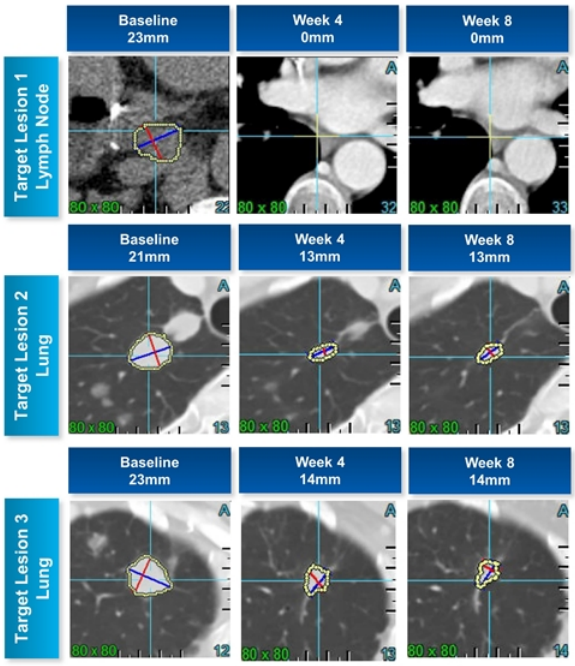
66-year-old female,

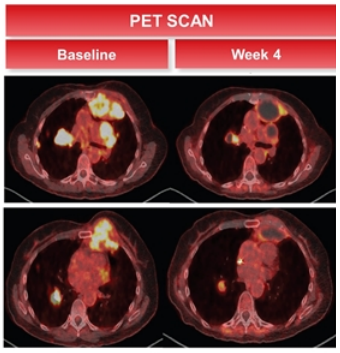
Relapsed pleural mesothelioma

- Failed 4 prior lines of therapy, including nivolumab/ipilimumab and anti-MSLN ADC

Enrolled in gavo-cel Clinical Trial Study

- **April 2021**: Lymphodepletion with Flu/Cy followed by gavo-cel at $5x10^8/m^2$





Case Study: Patient 5 – Ovarian Cancer

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

70-year-old female,

High grade, Stage IV serous ovarian cancer

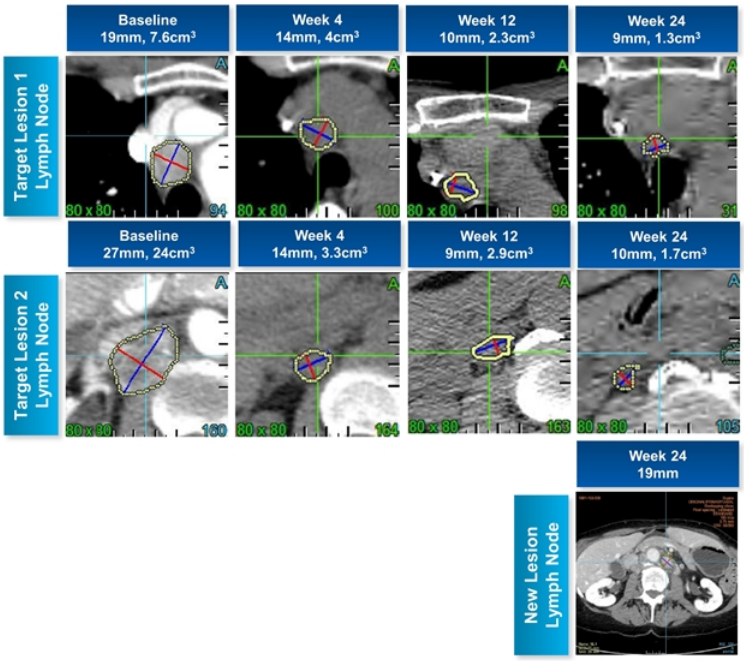
- *TP53*^{R248Q}, *CCNE1* amplified, wild type *BRCA1/2*
- Failed 6 prior lines of therapy
- Platinum resistant

Enrolled in gavo-cel Clinical Trial Study

- **April 2020**: Lymphodepletion with Flu/Cy followed by gavo-cel at 5x10^7/m^2

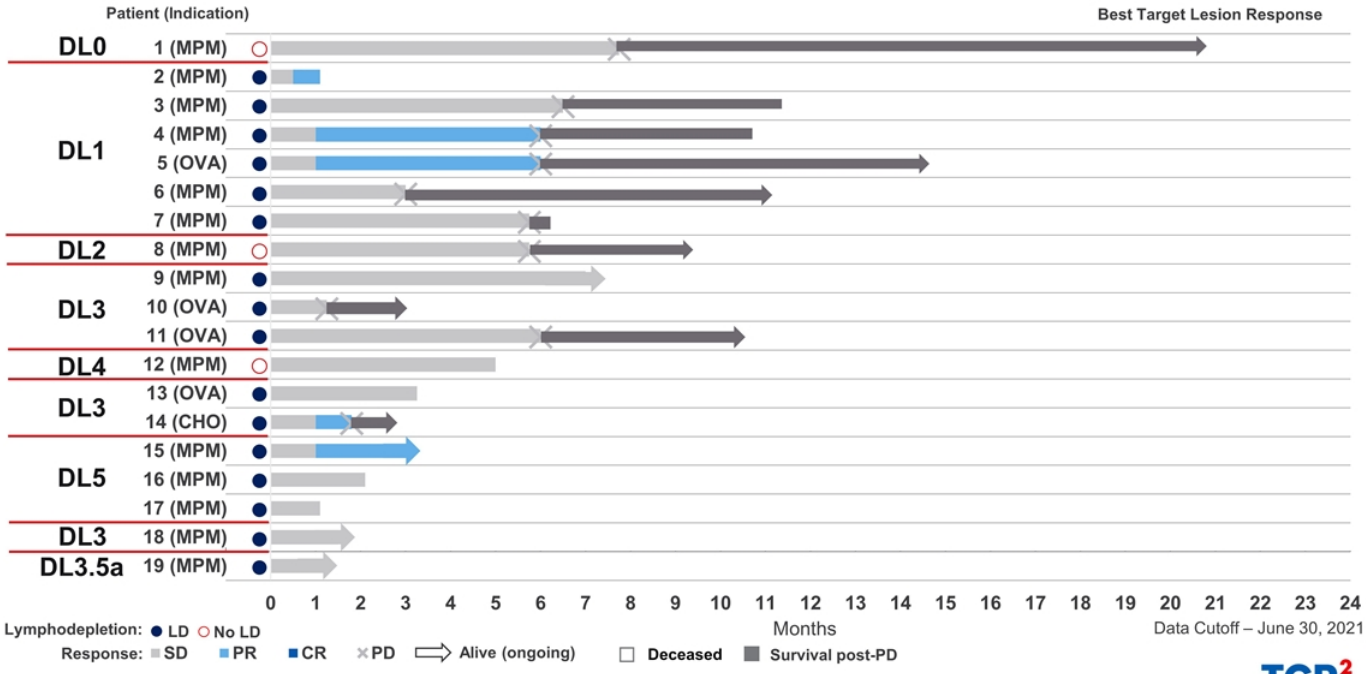
Response Post gavo-cel

- Target Lesions: **PR (at months 1, 2, 3, 6)**
- Non-target Lesions: **CR (at months 1, 2, 3, 6)**
- Best overall assessment: **PR (at month 3)**
- Overall: **PD** (new lymph node lesion)



Patient Response and Follow-Up

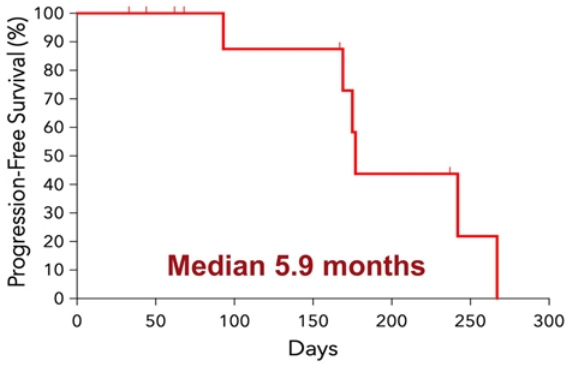
Overall Response Rate 25%, Disease Control Rate 81%



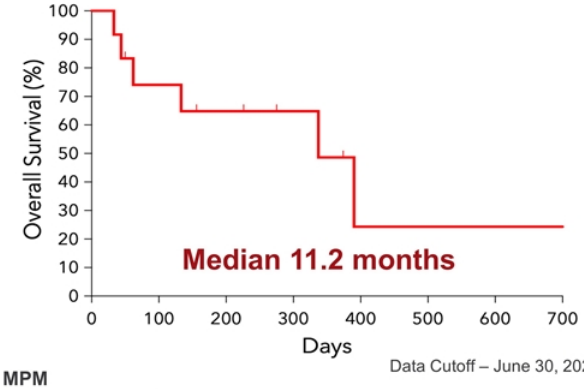
Survival of Patients with Mesothelioma

gavo-cel in Patients with MPM: ORR 38%, PFS 5.9 Months, OS 11.2 Months

gavo-cel Progression Free Survival



gavo-cel Overall Survival



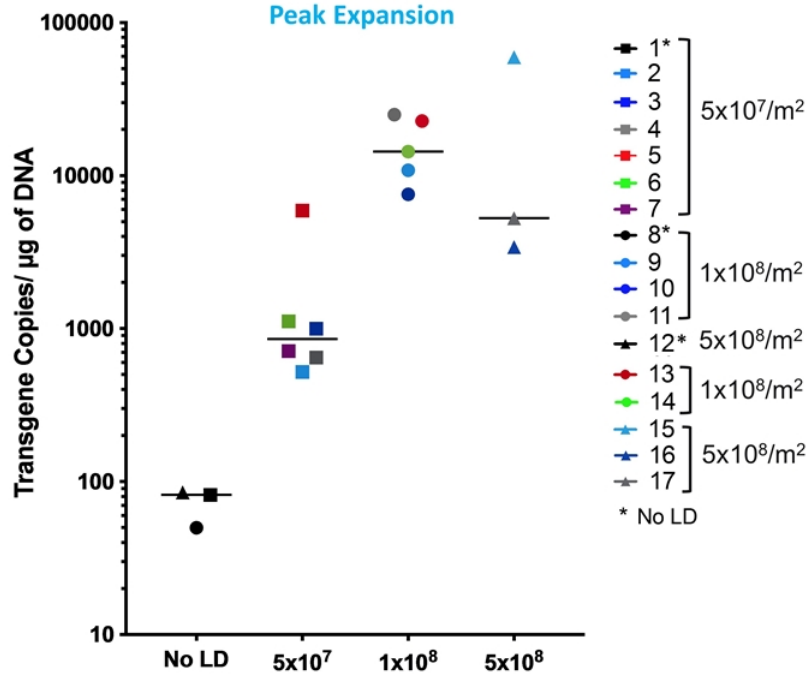
Data Cutoff – June 30, 2021

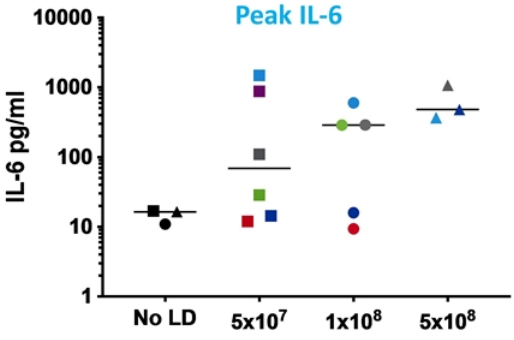
Second Line MPM
(Post Platinum-Based Frontline Therapy)

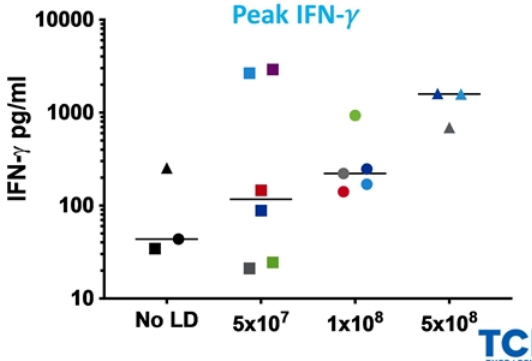
Monotherapy	n	ORR (%)	PFS (mo)	OS (mo)
Vinorelbine	98	3.1	4.2	9.3
vs **Supportive Care[1]**	56	1.8	2.8	9.1
Pembrolizumab	73	22	2.5	10.7
vs **Vinorelbine or Gemcitabine[2]**	71	6	3.4	12.4

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

gavo-cel Peak Expansion and Plasma Cytokine Levels







Clinical Trial Summary and Next Steps

Key Clinical Findings

- MTD identified ($5x10^8/m^2$ with LD)
  - Currently testing $3x10^8/m^2$ with LD to refine RP2D
- Clinical activity observed in all 3 solid tumor indications tested (DCR 81%, ORR 31% with LD)
- Meaningful ORR (38% with LD) and survival signal in mesothelioma
- Lymphodepletion linked to higher peak expansion and greater tumor regression

Next Steps

- Identification of RP2D
- Initiate Phase 2 expansion portion
  - Assess gavo-cel efficacy in four indications
  - Evaluate combinations with anti-PD1 antibody
  - Allow gavo-cel retreatment on progression or if stable disease
  - Test alternate mesothelin expression cutoff

MTD, maximum tolerated dose; LD, lymphodepletion; RP2D, recommended Phase 2 dose

Mesothelin Solid Tumors Represent a Significant Market

Initial gavo-cel Indications

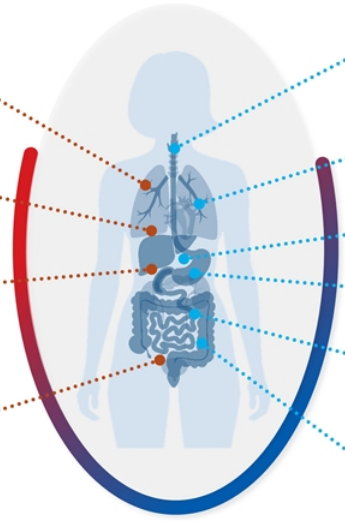
Population: 80,000 patients

Malignant Pleural Mesothelioma
Population: 2,100
Potential Accelerated Approval
✓ Orphan Drug Designation
76%

Non-Small Cell Lung Cancer
Population: 61,000
31%

Cholangiocarcinoma
Population: 4,000
Potential Accelerated Approval
✓ Orphan Drug Designation
50%

Ovarian Cancer
Population: 13,000
58%



Expansion Opportunities

Population: 163,000 patients

30% **Esophageal Cancer**
Population: 5,000

36% **Triple Negative Breast Cancer**
Population: 15,000

66% **Pancreatic Cancer**
Population: 38,000

40% **Gastric Cancer**
Population: 11,000

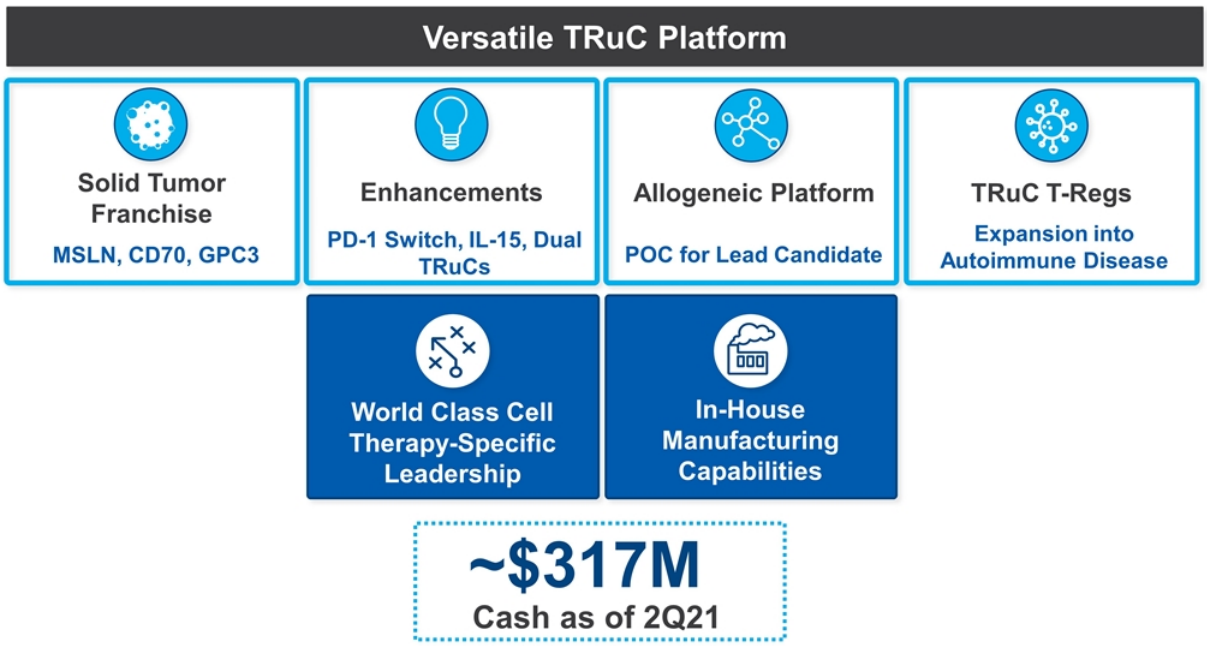
20% **Endometrial Cancer**
Population: 13,000

55% **Colorectal Cancer**
Population: 81,000

Percent of Patients with Mesothelin Surface Expression

Refs: Inaguma 2017, SEER Statistics 2020, Morello 2016, Tozbikian 2014

The Path Forward – Powering a Solid Tumor Franchise



~$317M
Cash as of 2Q21

TRuC, T Cell Receptor Fusion Construct; MSLN, mesothelin; POC, proof of concept

R&D Day – October 20, 2021

- Further update on gavo-cel clinical trial and Phase 2 strategy
- Individual program reviews and pipeline strategy
- Allogeneic development candidate and strategy/timelines
- Development and data for TRuC T-reg T cells

TCR² THERAPEUTICS

POWERING THE TCR

TO TRANSFORM THE LIVES OF CANCER PATIENTS WITH SOLID TUMORS

Thank You