#### 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 Exchange Act of 1934

Date of Report: (Date of earliest event reported) September 17, 2021

	GT Biopharma, Inc.	
(I	Exact name of registrant as specified in its charter)	·
	<u>Delaware</u> (State or other Jurisdiction of Incorporation)	
1-40023		94-1620407
(Commission File Number)	(IRS	S Employer Identification No.)
(Ac	9350 Wilshire Blvd., Suite 203 <u>Beverly Hills, CA 90212</u> ddress of Principal Executive Offices and zip code)	
(At	duces of Filherpai Executive Offices and zip code)	
(R	(800) 304-9888 egistrant's telephone number, including area code)	
Check the appropriate box below if the Form 8-K filing is intend	ed to simultaneously satisfy the filing obligation of re	egistrant under any of the following provisions:
<ul> <li>□ Written communications pursuant to Rule 425 under the Se</li> <li>□ Soliciting material pursuant to Rule 14a-12(b) under the Ex</li> <li>□ Pre-commencement communications pursuant to Rule 14d-</li> <li>□ Pre-commencement communications pursuant to Rule 13e-</li> </ul>	change Act (17 CFR 240.14a-12(b)) 2(b) under the Exchange Act (17 CFR 240.14d-2(b))	
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, \$0.001 par value	GTBP	The NASDAQ Stock Market LLC
Indicate by check mark whether the registrant is an emerging g Securities Exchange Act of 1934 (17 CFR 240.12b-2).	growth company as defined in Rule 405 of the Secur	rities Act of 1933 (17 CFR 230.405) or Rule 12b-2 of the
		Emerging growth company $\Box$
If an emerging growth company, indicate by check mark if the accounting standards provided pursuant to Section 13(a) of the E		on period for complying with any new or revised financial

#### Item 8.01. Other Events.

On September 17, 2021, Dr. Jeffrey Miller, a Professor of Medicine, University of Minnesota Medical School, Division of Hematology, Oncology and Transplantation and the Registrant's consulting Chief Scientific Officer, presented information regarding the Registrant's drug candidates at the European Society for Medical Oncology Congress 2021. Dr. Miller's presentation is filed as Exhibit 99.1 and is incorporated herein by reference.

The Registrant's updated corporate presentation as of September 20, 2021, which has been posted to the Registrant's website, is filed as Exhibit 99.2 and is incorporated herein by reference.

#### Item 9.01 Financial Statements and Exhibits.

#### (d) Exhibits.

99.1 Dr. Jeffrey Miller Presentation as of September 17, 2021.

99.2 GT Biopharma, Inc. Corporate Presentation as of September 20, 2021.

#### SIGNATURE

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.

#### GT BIOPHARMA, INC.

Date: September 23, 2021 By: /s/ Michael Handelman

Michael Handelman Chief Financial Officer



GTB-3550 TriKE™ safely activates and delivers IL-15 to NK cells, but not T cells, in immune suppressed patients with advanced myeloid malignancies, a novel paradigm exportable to solid tumors expressing HER2 or B7H3

J. Miller<sup>1</sup>, E. Warlick<sup>1</sup>, D. Vallera<sup>2</sup>, R. Wangen<sup>3</sup>, N. Zorko<sup>4</sup>, P. Hinderlie<sup>1</sup>, D. Lewis<sup>1</sup>, M. Felices<sup>1</sup>; 
<sup>1</sup>Medicine, Masonic Cancer Center – University of Minnesota, Minneapolis, MN, United States of America, <sup>2</sup>Radiation Oncology, Masonic Cancer Center – University of Minnesota, Minneapolis, United States of America, <sup>3</sup>Masonic Cancer Center, Masonic Cancer Center – University of Minnesota, Minneapolis, MN, United States of America, Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis, United States of America





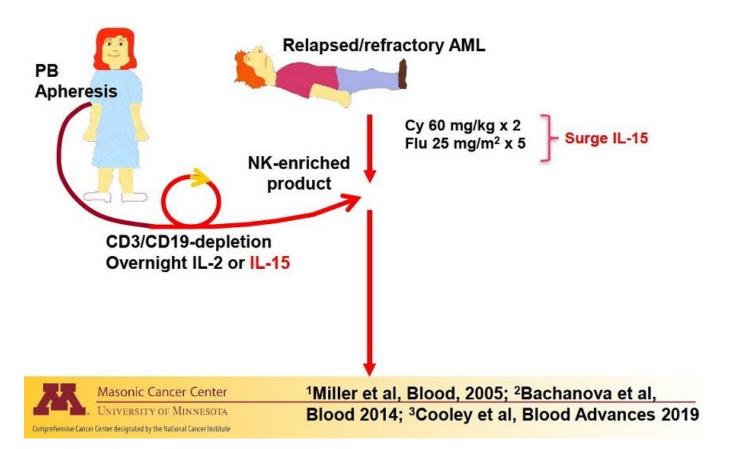
Comprehensive Cancer Center designated by the National Cancer Institute

# **Disclosures**

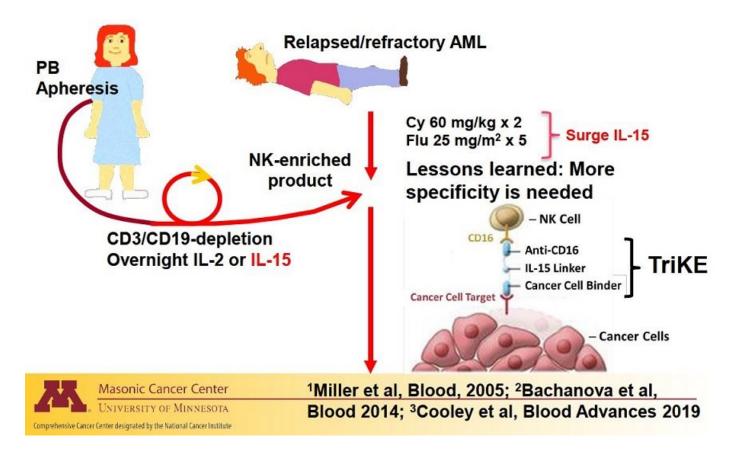
- GT BioPharma
  - SAB, Research Support, Consulting, Stock options
- Fate Therapeutics
  - Research Support, Consulting, Stock options
- Onklmmune, Nektar
  - SAB
- Vycellix
  - Consulting, Stock options



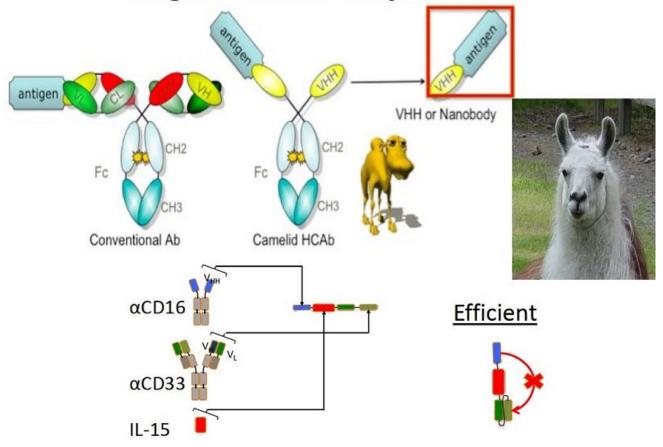
# Allogenic NK Cell Adoptive Transfer: Two Decades and Hundreds of Patients



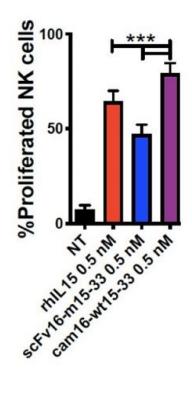
# Allogenic NK Cell Adoptive Transfer: Two Decades and Hundreds of Patients

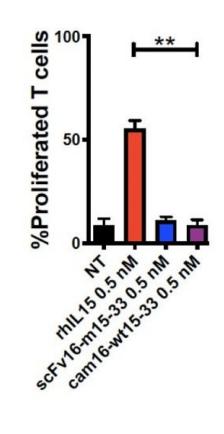


# Replacement Of scFv With Camelid VHH Single Domain Sequences

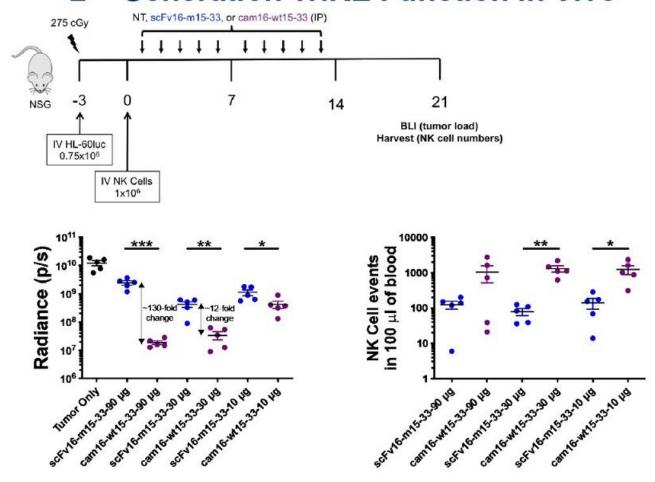


# camTriKE better activates NK Cells but not T Cells

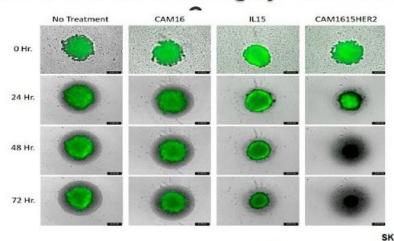


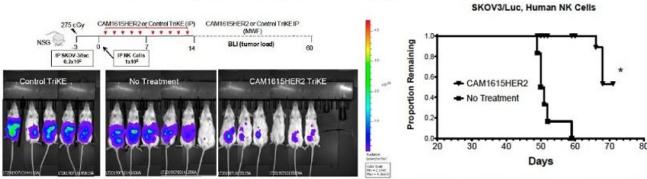


# 2<sup>nd</sup> Generation TriKE Function In Vivo



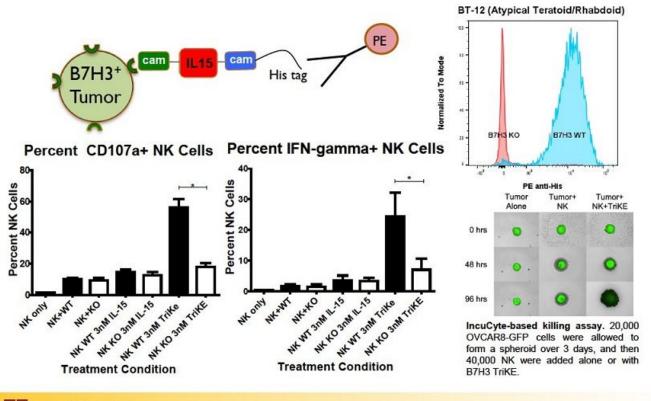
# Cam16/IL15/scFv HER2 TriKE Highly Effective Against Ovarian







# cam1615camB7H3 TriKE Pan Solid Tumor Targeting





# **Team Science**

## **University of Minnesota**

<u>Laboratory</u>	Faculty/MDs	<b>GMP Facility</b>
Martin Felices	Mark Juckett	David McKenna, MD
Daniel Vallera	Daniel J Weisdorf	Darin Sumstad
Frank Cichocki	John Wagner	Diane Kadidlo
Nick Zorko	Bruce Blazar	William Sharkey
Bruce Walcheck	Claudio Brunstein	Andy Sicheneder
Aimee Merino	Veronika Bachanova	

Bin Zhang Melissa Geller Todd Lenvik Joseph Maakaron

Zachary Davis Pippa Kennedy Upasana Arvinda Emily Chiu

Jake Myers







# Target Directed NK Cell Immunotherapy NASDAQ: GTBP

20 September 2021

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#### FORWARD LOOKING STATEMENT

This presentation includes statements that are, or may be deemed, "forward-looking statements." In some cases, you can identify forward-looking statements by terminology including "anticipates," "believes," "can," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "should," "will," "would" or the negative thereof, other variations thereon or other comparable terminology. We operate in a very competitive and rapidly-changing environment and new risks emerge from time to time. As a result, it is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. You are cautioned not to place undue reliance upon such forward looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements will be achieved or occur. We direct you to our Annual Report on Form 10-K for the year ended December 31, 2020, our subsequent current reports on Form 8-K, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, and our other filings with the Securities and Exchange Commission. Any forward-looking statement included in this presentation speaks only as of the date hereof. Except as required by law, we do not undertake any obligation to update or revise, or to publicly announce any update or revision to, any of the forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

This presentation is made pursuant to Rule 163B under the Securities Act of 1933, as amended, and is intended solely for investors that are either qualified institutional buyers or institutions that are accredited investors (as such terms are defined under Securities and Exchange Commission rules) solely for the purpose of determining whether such investors might have an interest in a securities offering contemplated by us. Any such offering of securities will only be made by means of a registration statement (including a prospectus) filed with the Securities and Exchange Commission, after such registration statement becomes effective. No such registration statement has become effective as of the date of this presentation. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. In the event we conduct an offering, before you invest, you should read the prospectus in the registration statement and other documents we file with the Securities and Exchange Commission for more complete information about us and the offering. You may get these documents for free by visiting EDGAR on the Securities and Exchange Commission website at http://www.sec.gov.



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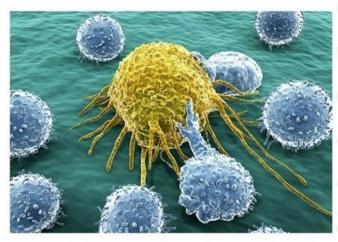
#### GT BIOPHARMA RECENT MAJOR MILESTONES





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#### COMPANY FOCUS - HARNESSING NATURAL KILLER CELLS TO FIGHT CANCER



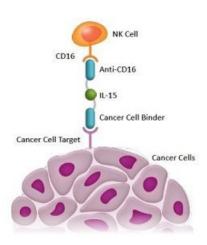
Source: Levy R. Paths of Progress 2019, Natural Killer Cells: How the immune system's first wave of defense may play a newfound role in cancer care; accessed: 6 September 2021 https://www.dana-forber.org/newsroom/publications/paths-of-progress-2019/natural-killer-cells/

- Restore patient's exhausted/inhibited endogenous NK cell population to again recognize and kill cancer cells.
- Natural Killer (NK) cells are cytotoxic lymphocytes of the innate immune system.
- NK cells are analogous to cytotoxic T-cells of the adaptive immune system.
- NK cells are early responders that recognizes and kills stressed cells in the absence of antibodies.
- Minimize toxicities such as cytokine release syndrome (CRS) resulting from hyperactivation of T-cells.
- TriKE® is an immune oncology protein therapeutic which activates NK cells, and directs them to specific cancer cell targets. TriKE® is not a cell therapy.



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#### WHAT IS A TRIKE® THERAPEUTIC?



#### **Key Therapeutic Features:**

- · Target-directed ADCC killing.
- Integrated cytokine support within the tumor micro-environment (TME).
- Simultaneous NK cell ADCC activation, proliferation and persistence.
- First-in-Class modular immune oncology protein therapeutic platform technology.



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Persistence means the ability of an NK cell population to exist at activated levels in the body for periods of several weeks, with each activated NK cell able to mediate the serial killing of multiple cancer cells.

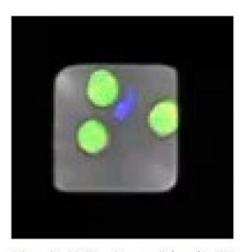
# TRIKE® PRODUCT CANDIDATE PIPELINE

TriKE® Product Candidates	Approach	Indication	Stage					Status
			Pre-Clinical	GMP Manufacturing	Phase 1	Phase 2	Phase 3	
GTB-3550	Monotherapy	Leukemia – AML, MDS						Phase 1
GTB-3650 2 <sup>nd</sup> Generation Camelid	Monotherapy	Leukemia – AML, MDS, MRD						Pre-IND
	Combination with Chemotherapy	Leukemia – AML, MDS, MRD						Pre-IND
GTB-4550 Camelid	Monotherapy & Combination	PD-L1 / Solid Tumor						Pre-IND
GTB-5550 Camelid	Monotherapy & Combination	B7H3 / Solid Turnor						Pre-IND
GTB-6550 Camelid	Monotherapy & Combination	HER2 / Breast and Gastric						Pre-IND
Undisclosed Candidates	Monotherapy & Combination	Solid and Liquid Tumors Infectious Disease						Pre-IND

GT BIOPHARMA

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#### TRIKE® DIRECTED NK CELL SERIAL KILLING OF AML CANCER CELLS



Enhanced Serial Killing of Cancer cells (green) by TriKE directed NK cell (blue).

Source: Sarhan D et al. Blood Adv 2018 Jun 26; 2(12): 1459-1469

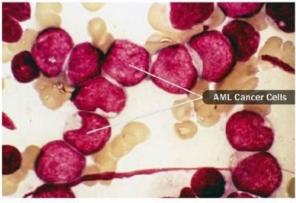
- · Integrated CD16 and IL-15 in TriKE drives:
  - NK cell ADCC activation for enhanced serial killing of cancer cells
  - > NK cell proliferation
  - > NK cell persistence
- TriKE minimizes toxicities such as cytokine release syndrome (CRS) resulting from hyperactivation of T-cells.
- TriKE therapeutics can be used to treat solid tumors and hematological cancers.
- TriKE is an immune oncology protein therapeutic

   not a cell therapy.



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#### GTB-3550 TRIKE® PRODUCT CANDIDATE



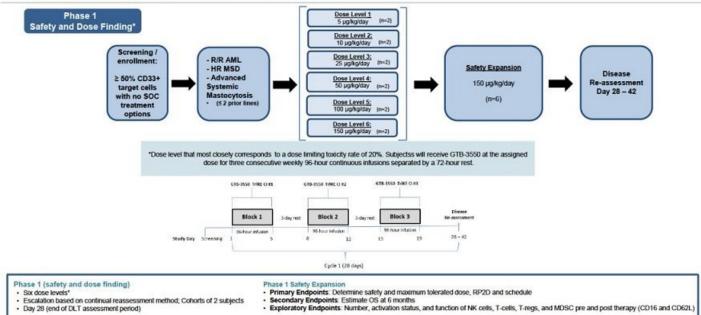
Source: Pr. J Bernard/CNRI/Science Source

- First-in-Class immune oncology therapy.
- Target-directed NK cell ADCC killing of CD33+ hematological cancers.
- Incorporates IL-15 within therapeutic for enhanced NK cell proliferation and persistence.
- Currently being evaluated in a First-in-Human Phase 1 clinical trial.



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#### TRIKE® GTB-3550 PHASE 1 STUDY DESIGN





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#### GTB-3550 FIRST IN HUMAN CLINICAL TRIAL INTERIM RESULTS

Subject	Dose level (µg/kg/d)	Disease and Prior Treatment History	Disease Characteristics Before GTB-3550 Therapy	Disease Characteristics After GTB-3550 Therapy	Response Post Cycle :
1	5	t/r AML Triple Hit lymphoma - 6 therapies: 1. R-EPOCHs6, 2. RICE x3, 3. XRT to abdominal lymphadenopathy, 4. NAM-NK Clinical Trial, 5. CAR-T, 6. andi-CD20 and Anti-CD3 monoclonal antibody clinical trial	Cellularity: 10% Blast: 5 – 10%	Cellularity: 10 - 30% Blast: 10%	Stable AML with improved platelet transfusion needs
2	5	r/r AML AML-3 therapies before TriKE: 1. Vyxeos + Midostaurin 2. FLAG-IDA + midostaurin 3. Decitabine + Gilteritinib	Cellularity: 70 – 80% Blast: 7%	Cellularity: 90 – 95% Blast: 94%	Progression
3	10	r/r AML AML- 3 therapies before TrikE: 1. Azacitidine, 2. Enasidenib, 3. Hydrea	Cellularity: 100% Blast: 85%	Cellularity: 100% Blast: 92%	Stable AML
4	10	t-MDS. Multiple Myeloma - 5 therapies: 1. CyBorD, 2. Bortezomib, 3. Dexamethasone + lenalidomide + idazomib, 4. Daratumumab + Pomalidomide + Dexamethasone, 5. Dara maintenance	Cellularity: 5% Blast: 5.5%	Cellularity: 5% Blast: 20%	Stable MDS
5	25	Secondary AML, progressed from MDS.	Cellularity: 10 – 15% Blast: 18%	Cellularity: 20% Blast: 12%	Blast count reduction, improved platelet needs
6	25	r/r AML 2 therapies before TriKE: 1.7+3 with CR1 then relapse, 2. Azacitidine + Venetoclax	Cellularity: 10 – 20% Blast: 29%	Cellularity: 10 – 20% Blast: 35%	Mild blast increase
7	50	HR MIDS. MIDS - 3 therapies: 1. Decitabine, 2. Luspatercept, 3. Decitabine 10 day	Cellularity: 70 – 80% Blast: 12%	Cellularity: 60% Blast: 4.6%	Partial remission
8	50	HR MDS, MDS - 3 therapies before TriKE1. Azacitidine, 2. NMA DUCBT, CR1 for 7 years before relapse 3. Azacitidine – CR2 then relapse	Cellularity: 20% Blast: 12%	Cellularity: 30% Blast: 19%	Mild blast increase
9	100	High Grade MDS-1. Azactistine. 2. Decitabine, 3. 7+3, 4. Alio transplant with CR then relapse and progression to AML then no response to Decitabine + Venetoclax	Cellularity: 20% Blast: 22%	Cellularity: 10 – 20% Blast: 8%	Partial remission
10	100	t/r AML Breast Cancer: 4 therapies: 1. Masectomy/LN dissection, 2. XRT, 3. Adriamycin/Cyclophosphamide, 4. Taxol.	Cellularity: 10% Blast: 17%	Cellularity: 40% Blast: 31%	Stable AML
11	150	DLBCL - 3 therapies 1. R-DA-EPOCH, 2. Auto Transplant, 3. ADAM-17-Ritanimab, Therapy-related MDS: 2 therapies: 1. Azactidine, 2. Allo transplant – CR, Relapse/transformed to AMI, (bi-phenotypic) - 1 therapy before TriCE: 1. Venetockax + Decitabine x 2 cycles	Cellularity: 25% Blast: 80%	Cellularity: 80% Blast: 73%	Blast reduction by FLOW
12	150	r/r AML - 2 therapies: 1. FLAG-IDA + venetoclax, 2. Decitabine	Cellularity: 30 – 40% Blast: 36%	Cellularity: 60 % Blast: 64%	Disease Progression

- · Patient 5: 33% reduction in blast count
- · Patient 7: 61.7% reduction in blast count
- · Patient 9: 63.6% reduction in blast count
- Patient 11: 50% reduction in CD33+ blast count

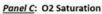


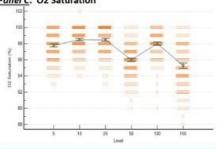
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## GTB-3550 TRIKE® IS SAFE AND WELL TOLERATED

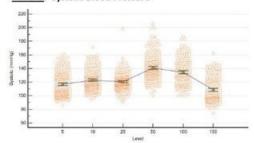
<u>Panel A</u>: Dose Equivalent of GTB-3550 and Systemic Maximum
Therapeutic Dose of IL-15

PER MOLE BASIS		
Dose of GTB-3550 (μg/kg)	Fold Higher than MTD rhIL-15	
5	0.54	
10	1.08	
25	2.69	
50	5.38	
100	10.75	
150	16.13	

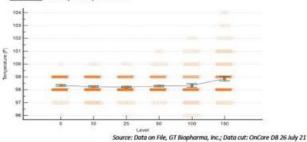




Panel B: Systolic Blood Pressure



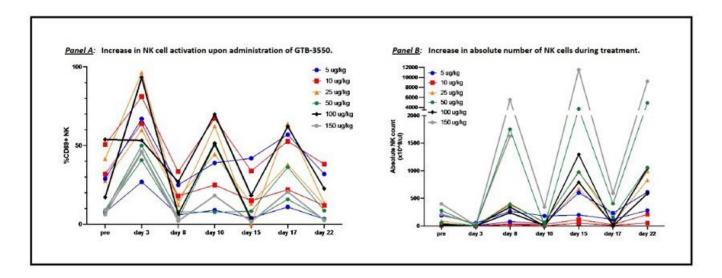
Panel D: Body Temperature





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# GTB-3550 TRIKE® ACTIVATES ENDOGENOUS NK CELLS IN THE PERIPHERY, EGRESS INTO TISSUES

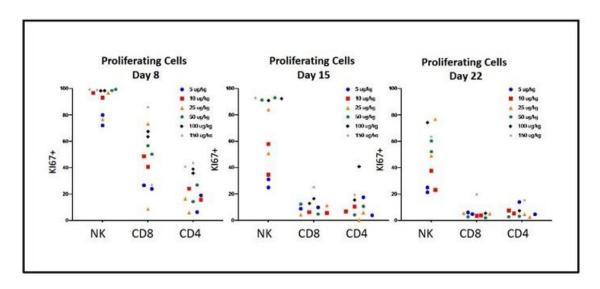


Source: Data on File, GT Biopharma, Inc.



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#### GTB-3550 TRIKE® DEMONSTRATES DOSE DEPENDENT & SUSTAINED PROLIFERATION OF ENDOGENOUS NK CELLS

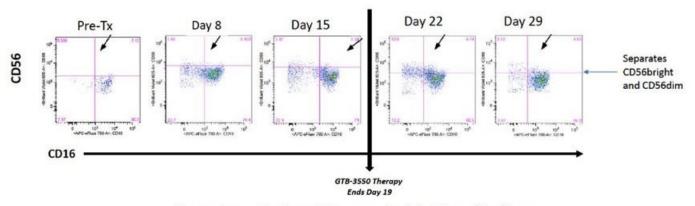


Source: Data on File, GT Biopharma, Inc.



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# No Loss of CD16 During GTB-3550 Therapy



Data from Patient #7 treated with 50 µg/kg/day

Source: Data on File, GT Biopharma, Inc.



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#### GTB-3550 TRIKE® FIRST-IN-HUMAN CLINICAL TRIAL INTERIM RESULTS

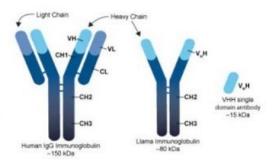
- GTB-3550 TriKE induces reproducible NK cell proliferation in all patients at all dose levels evaluated with no clinically significant toxicity. No CRS resulting from hyperactivation of patient's T-cell population at doses  $5-100~\mu g/kg/day$ . Grade 1 CRS observed in 150  $\mu g/kg/day$  in one subject enrolled.
- Clinical responses to date demonstrate strong NK cell activation, persistence, proliferation and targeted cancer cell killing.
- GTB-3550 significantly reduced bone marrow blast levels 33.3%, 61.7%, 63.6%, and 50% (CD33+) in Patient 5 (25 μg/kg/day), Patient 7 (50 μg/kg/day), Patient 9 (100 μg/kg/day), and Patient 11 (150 μg/kg/day), respectively.
- · No loss in CD16 expression on patient's NK cells.



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#### CAMELID ANTIBODIES - SECOND GENERATION TRIKE®

- Camelid antibodies are antibodies from the Camelidae family of mammals that include llamas, camels, and alpacas.
- Camelid antibody is made up of only 2 heavy chains. This is known as heavy chain IgG (hclgG). While these antibodies do not contain the CH1 region, they retain an antigen binding domain called the V<sub>H</sub>H region.
- V<sub>H</sub>H antibodies, also known as single domain antibodies or Nanobodies\*, contain only the V<sub>H</sub>H region from the camelid antibody.
- Therapeutic and Commercial Advantages of Second Generation (GTB-3650, others) as Compared to First Generation (GTB-3550)
  - · Improved potency and enhanced binding affinity
  - · Commercial manufacturing capabilities through Cytovance
  - · Proprietary molecule wholly owned by GT Biopharma
  - · Similar preclinical safety profile



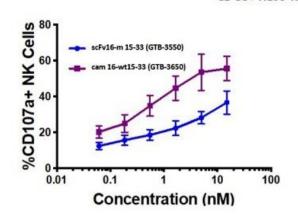
Source: https://www.rndsystems.com/products/llamabody-camelid-antibodies

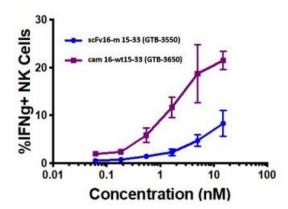


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# SECOND GENERATION TRIKE® (CAMELID) IMPROVES NK FUNCTION

CD 33+ HL60 Targets



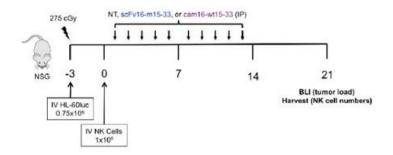


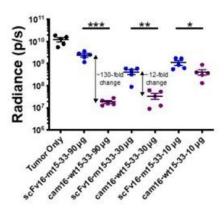
Source: Modified, Felices M et al. Cancer Immunol Res 2020 Sep; 8(9): 1139-1149



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# SECOND GENERATION TRIKE® (CAMELID) SUPERIOR IN-VIVO



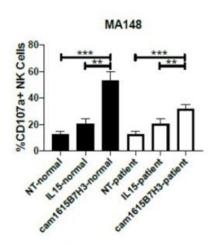


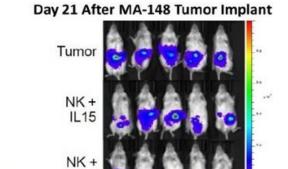
Source: Felices M et al. Cancer Immunol Res 2020 Sep; 8(9): 1139-1149

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#### PIPELINE TRIKE® B7H3: PAN CANCER SOLID TUMOR TARGETING





Dosing: 5x/week (MTWThF) Schedule: 3 weeks

Significant killing of MA148 Ovarian Cancer by TriKE® B7H3

TriKE® B7H3

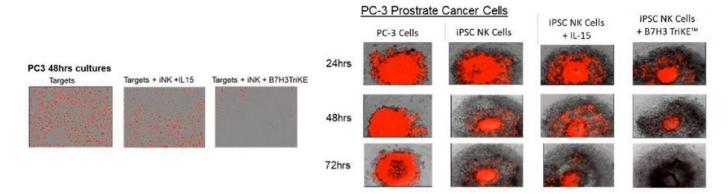
Source: Vallera DA et al. Cancer 2020 Sep 18;12(9):2659



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#### TRIKE® MAKES NK CELL THERAPIES MORE EFFECTIVE

## Clear Competitive Advantage in Solid Tumor Cancers



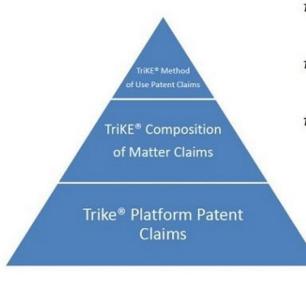
J Immunother Cancer (2020) Vol. 8 (Suppl 3), Abstract 470, pg. A287. Presented at Society of Immunotherapy Cancer (SITC), November 2020.

<sup>1</sup>Jeffrey Miller, <sup>1</sup>Nicholas Zorko, <sup>1</sup>Behiye Kodal, <sup>1</sup>Zachary Davis, <sup>1</sup>Alexander Lenvik, <sup>1</sup>Fodd Lenvik, <sup>1</sup>Joshua Walker, <sup>1</sup>Daniel Vallera, <sup>2</sup>Svetlana Gaidarova, <sup>2</sup>Alejandro Garcia, <sup>2</sup>Tom Lee, <sup>2</sup>Ryan Bjordahl, <sup>2</sup>Bahram Valamehr, <sup>1</sup>Frank Cichocki, <sup>4</sup>Martin Felices. <sup>1</sup>University of Minnesota, Minneapolis, MN, USA; <sup>2</sup>Fate Therapeutics, Inc., San Diego, CA, USA



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#### MULTI-LAYERED PATENT STRATEGY



#### TriKE® Method of Use Patent Claims

 Methods of use claims highlighting coverage for oncology and infectious disease therapeutic applications.

#### TriKE® Composition of Matter Patent Claims

 Composition of matter claims covering DNA and amino acid sequences for all TriKE™ therapeutic product opportunities.

#### TriKE® Platform Patent Claims

- Claims focused on simultaneously engaging and activating NK cells using a single therapeutic construct incorporating IL-15 to minimize toxicity and the need for co-administration of IL-15.
- Claims focused on target-directed NK cell killing and IL-15 trafficking to TMF.

#### Two New Patents Issued (24 August 2021) Covering TriKE® Platform

- Patent No. 11,098,100 broad coverage for CD16, IL-15, and any targeting domain
- 2. Patent No. 11,098,101 broad coverage for any HIV target antigen



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#### TriKE® Competitive Advantages

- The anti-CD16 component of the TriKE binds FcRγIII at high affinity compared to ADCC mediated strategies that bind at low affinity.
- CD16 +/- other receptor engagement does not result in proliferation of T-cells contributing to CRS.
- IL-15 provides NK cell specific proliferation with less bystander activity and has a greater safety profile than cytokine therapy.
- TriKE can be targeted to heme malignancies, solid tumors and infectious diseases.
- Overall therapeutic regimen costs the same as today's antibody therapies.







NK cell engager/antibody therapeutic strategies designed to engage CD16, NKG2D, or NKp30, but none of them co-stimulate CD16 and IL-15 simultaneously.







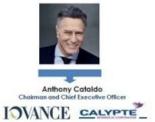
NK cell therapy. Significantly more expensive.



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#### EXPERIENCED MANAGEMENT TEAM

PROVEN RECORD IN BIOTECH, PHARMA, PRODUCT DEVELOPMENT, FINANCING





Gregory Berk, MD President R&D and Chief Medical Officer Verastem intellikine























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# Target Directed NK Cell Immunotherapy NASDAQ: GTBP

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