

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)
November 1, 2021

GT Biopharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other Jurisdiction of Incorporation)

1-40023
(Commission File Number)

94-1620407
(IRS Employer Identification No.)

9350 Wilshire Blvd., Suite 203
Beverly Hills, CA 90212
(Address of Principal Executive Offices and zip code)

(800) 304-9888
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of 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(b) under the Exchange Act (17 CFR 240.14a-12(b))
☐ 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 240.13e-4(c))

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

<u>Title of each Class</u>	<u>Trading Symbol(s)</u>	<u>Name of each Exchange on which registered</u>
Common stock, \$0.001 par value	GTBP	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 (17 CFR 230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR 240.12b-2).

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 8.01. Other Events.

The Registrant's updated corporate presentation as of November 1, 2021, which has been posted to the Registrant's website, is filed as Exhibit 99.1 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<u>99.1</u>	<u>GT Biopharma, Inc. Corporate Presentation as of November 1, 2021.</u>
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SIGNATURE

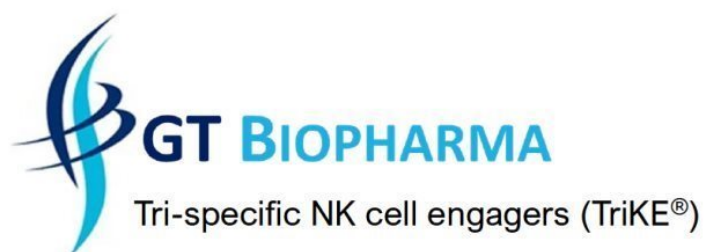
Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

GT BIOPHARMA, INC.

Date: November 1, 2021

By: /s/ Michael Handelman

Michael Handelman
Chief Financial Officer



*Utilizing novel camelid nanobody platform technology with
target-directed immunotherapy for cancer*

November 1, 2021

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 are reasonable, we 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. 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, whether as a result of new information, future events or any other reason after the date of this presentation. For all 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>.

GT Biopharma Snapshot

Corporate Profile

GT Biopharma is a clinical stage immuno-oncology company focused on its proprietary Tri-Specific Natural Killer Cell Engager or TriKE® platform technology.

TriKE's are comprised of camelid nanobody based immune cell engagers which activate natural killer (NK) cells in order to selectively target and kill tumor cells.

Scalable platform with a pipeline of multiple TriKE's targeting various solid tumors and hematological malignancies.

Stock Information

Stock Price (as of October 29, 2021)	\$6.46
Shares Outstanding (as of June 30, 2021)	31.5M
Warrants (cash exercise; \$5.50 strike)	~2.0M
Market Cap (as of October 29, 2021)	\$204M
Cash, cash equivalents (as of June 30, 2021)	\$39.5M

Timeline of Events

Jul 2014	Mar 2019	Oct 2019	Feb 2020	Oct 2020	Feb 2021	Jun 2021	Jul 2021	Sep 2021
GTB founded	Management restructuring Anthony Cataldo named CEO	HIV TriKE® data demonstrates NK cell Killing	GTB-3550 1st patient dosed in Phase 1/2 AML and MDS trials	Results of B7H3 targets multiple cancers	Debut on NASDAQ	GTB Added to Russell 2000	\$16 MM Warrant Exercise	GMP initiated for 2 nd generation TriKE®s

Investment Opportunity – Next Generation of NK Cell Engagers for Cancer

Proprietary TriKE® Platform – Camelid Nanobodies

- TriKE® platform creates tri-specific NK cells engagers targeting multiple tumor types
- Camelid “nanobodies” – now known as “third generation antibodies”
- Smallest known functional antibody fragment particularly well suited for cancer therapeutics

NK Cell Engagers – Safer than T Cells¹

- Harness the natural killing power of NK cells with protein therapeutics – NOT NK cell therapy
- Induce activation of NK cells via CD16A and IL-15 while targeting well-known tumor antigens
- Offers a potentially safer alternative to T-cell related immunotherapy without CRS & neurotoxicity

POC Established and Broad Applicability

- GTB-3550 (targeting CD33) has now shown POC data in Phase 1 with AML patients
- GTB-3650 will supplant 3550 as 2nd generation TriKE with several advantages
- TriKE's targeting multiple tumor antigens including B7H3, HER2, CD33, PDL1

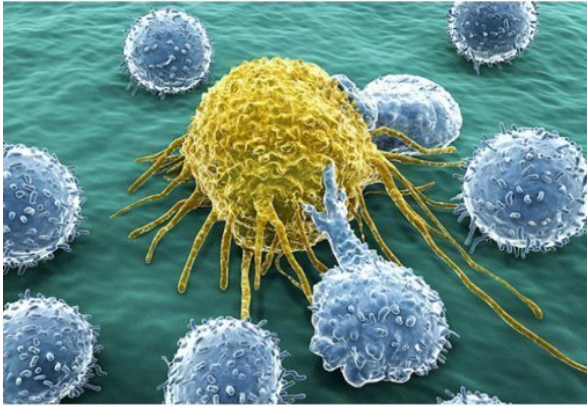
Multiple Catalysts

- 6+ pipeline assets in active preclinical development targeting both solid tumors and hematological malignancies

Well-funded Experienced Leadership

- Management team with deep expertise in all stages of oncology drug development
- \$40M in cash provides ample runway into 2023

Natural Killer Cell Engagers to Fight Cancer



Natural Killer Cells

- Cytotoxic lymphocytes in the innate immune system
- Recognize and kill cancer cells
- Mediate antibody-dependent cellular cytotoxicity (ADCC) via the highly potent CD16 activating receptor

NK Cell Engagers

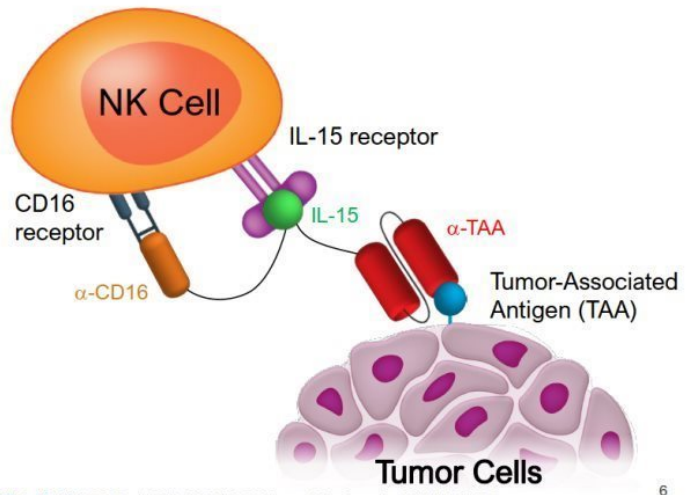
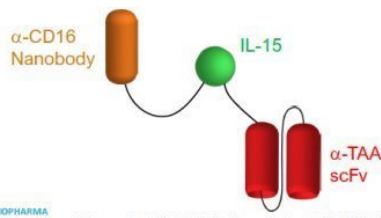
- TriKE® nanobody platform designed to activate endogenous NK cells to target specific cancer cells
- Potential for less toxicity than other cellular therapies such as CAR-T therapy
 - Less cytokine release syndrome (CRS)
 - Fewer neurological complications

TriKE®: Tri-Specific Natural Killer (NK) Cell Engagers – Modular Platform

Proprietary platform utilizing camelid nanobody technology designed to bridge NK cells to tumor cells while inducing NK cell activation and expansion at the site of the tumor to enhance killing

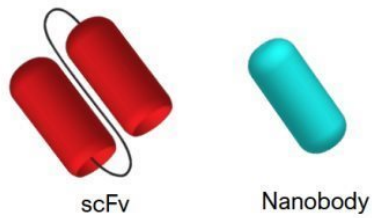
Tri-specific Modular Platform with Nanobody Technology

- **Anti-CD16 nanobody*** – binds CD16 receptor on NK cells, triggering antibody directed cell-mediated cytotoxicity (ADCC)¹
- **IL-15** – crosslinker that binds IL-15/IL-2 receptor on NK cells to induce self-sustaining expansion and extended survival^{2,3}
- **Anti-TAA scFv** – scFv domain binds to various tumor-associated antigens on tumors



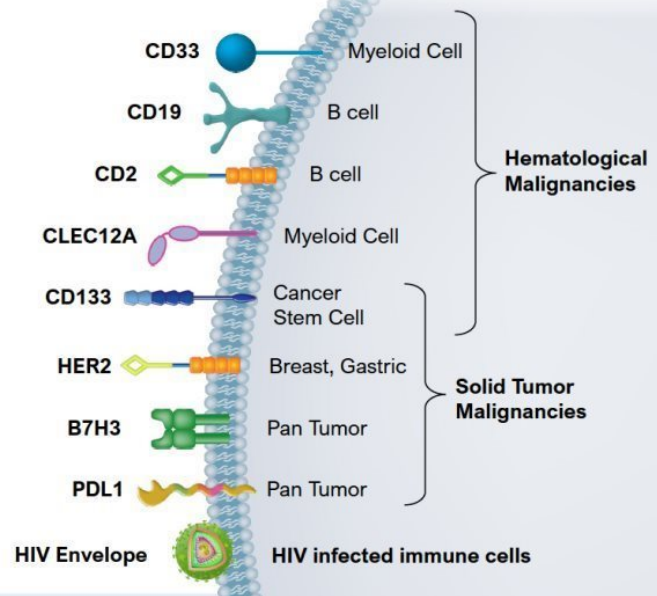
* 1st generation TriKE GTB3550 utilizes scFv for α-CD16. 1. *Semin Immunol*. 2017 Jun; 31: 64–75. 2. *J Exp Med*. 1994 Oct 1; 180(4): 1395–1403. 3. Valleria et. al. *Clin Cancer Res*. 22(14) July 15, 2016

TriKE® Modular Platform Allows for Multiple Tumor-Associated Antigen Targeting



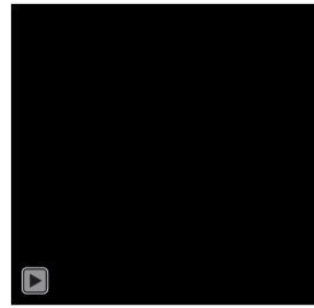
Anti-Tumor Associated Antigen

- Binds to well-known tumor-specific antigens
- Defines the specificity of each TriKE®
- Localizes NK cells at the site of the malignancy
- Utilizes scFv fragments for most TriKE® constructs
- Certain TriKE®s utilize nanobodies for the α -TAA



TriKE® – NK Cell-Driven Serial Killing of AML Tumor Cells

- First-in-class modular immune oncology protein therapeutic platform technology – not a cell therapy
- Target-directed antibody-dependent cellular cytotoxicity (ADCC) killing
- Integrated CD16 and IL-15 driven activation of NK cells:
 - ADCC activation for enhanced serial killing of cancer cells
 - NK cell proliferation
 - NK cell persistence
- Minimizes toxicities such as cytokine release syndrome (CRS) resulting from hyperactivation of T cells
- Can be used to treat BOTH solid tumors and hematological cancers



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

TriKE® Nanobody Pipeline

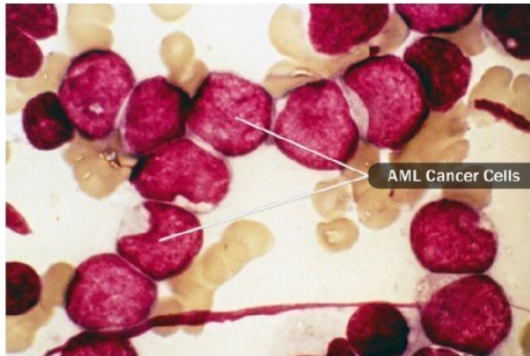
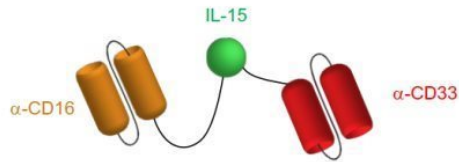
TriKE® Product Candidates	Approach	Target	Indication	Pre-Clinical	IND-Enabling/ GMP Manufacturing	Phase 1	Phase 2
GTB-3550	Monotherapy	CD33	Leukemia – AML, MDS				
GTB-3650 2 nd Generation Camelid	Monotherapy	CD33	Leukemia – AML, MDS				
	Combination with Chemotherapy	CD33	Leukemia – AML, MDS				
GTB-5550	Monotherapy & Combination	B7H3	Solid Tumors				
GTB-6550	Monotherapy & Combination	HER2	Solid Tumors				
GTB-4550	Monotherapy & Combination	PDL1	Solid Tumors				
GTB-1050	Monotherapy & Combination		HIV				
Undisclosed Candidates	Monotherapy & Combination		Solid & Hematological Malignancies				



GTB-3550 for AML and MDS

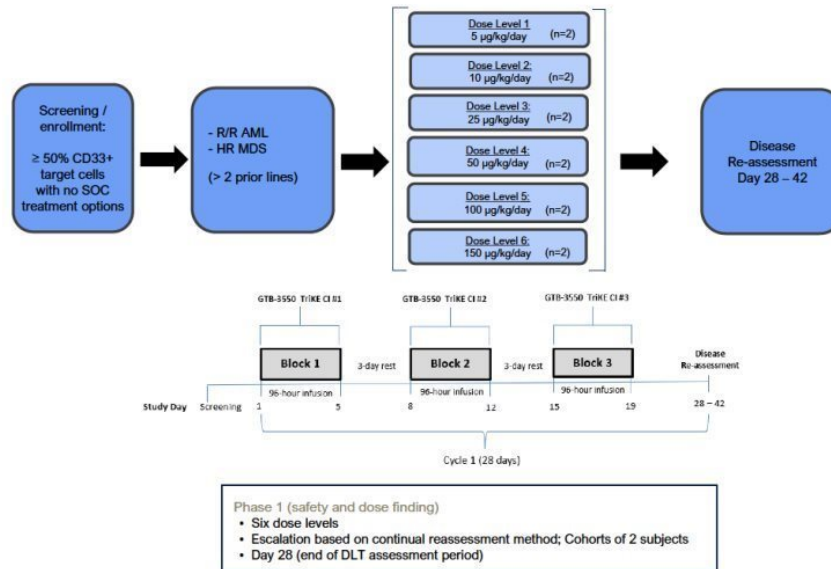
First generation TriKE® provides POC for platform

GTB-3550 TriKE® – Has Now Established Initial Proof of Concept in Phase 1 AML Trial



- First-in-class immune oncology therapy
- Target-directed NK cell ADCC killing of CD33+ hematological cancers
- Incorporates IL-15 within the TriKE® for enhanced NK cell proliferation and persistence
- Currently being evaluated in a first-in-human Phase 1 clinical trial
- Will be supplanted by 2nd generation GTB-3650

GTB-3550 Phase 1 Study Design



GTB-3550 First in Human Phase 1 Clinical Trial – Individual 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
1	5	r/r AML Triple Hit Lymphoma - 6 therapies: 1. R-EPOCHx6, 2. RICE x3, 3. XRT to abdominal lymphadenopathy, 4. NAM-NK Clinical Trial, 5. CAR-T, 6. anti-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 MDS MDS - 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. Azacitidine, 2. Decitabine, 3. 7+3, 4. Allo 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	r/r AML Breast Cancer: 4 therapies: 1. Mastectomy/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+Rituximab, Therapy-related MDS: 2 therapies: 1. Azacitidine, 2. Allo transplant – CR, Relapse/transformed to AML (bi-phenotypic) - 1 therapy before TriKE: 1. Venetoclax + 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

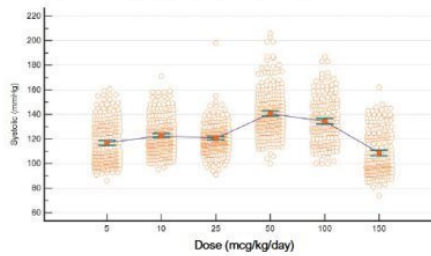
- Patient 5: 33% reduction in blast count
- Patient 7: 61.7% reduction in blast count
- Patient 9: 63.6% reduction in blast count
- Patient 11: 50% reduction in CD33+ blast count

GTB-3550 Safety Profile: Well-Tolerated & Minimal Cytokine Release Syndrome (CRS)

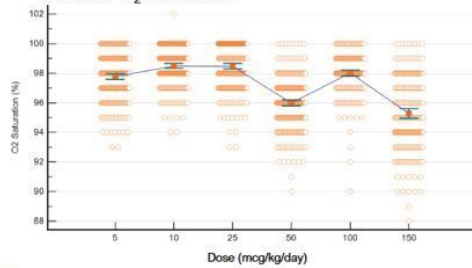
Panel A: Dose equivalent of GTB-3550 compared to recombinant human IL-15

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

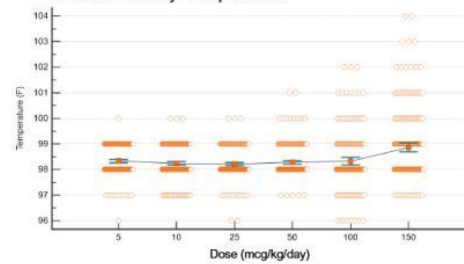
Panel B: Systolic Blood Pressure



Panel C: O₂ Saturation

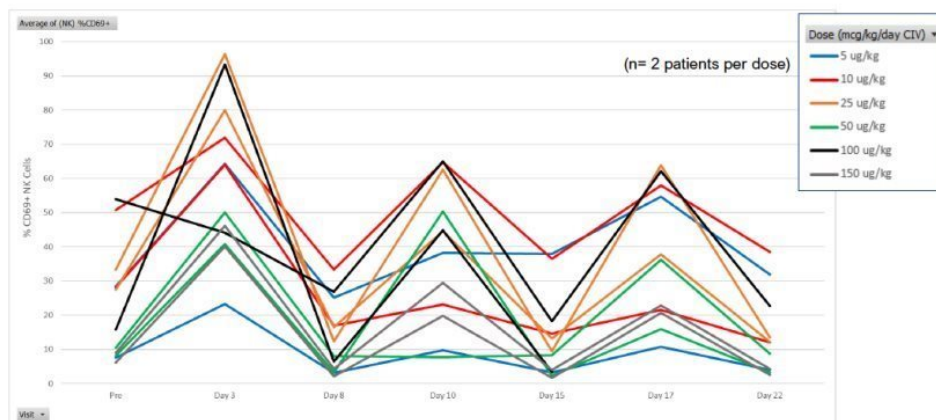


Panel D: Body Temperature

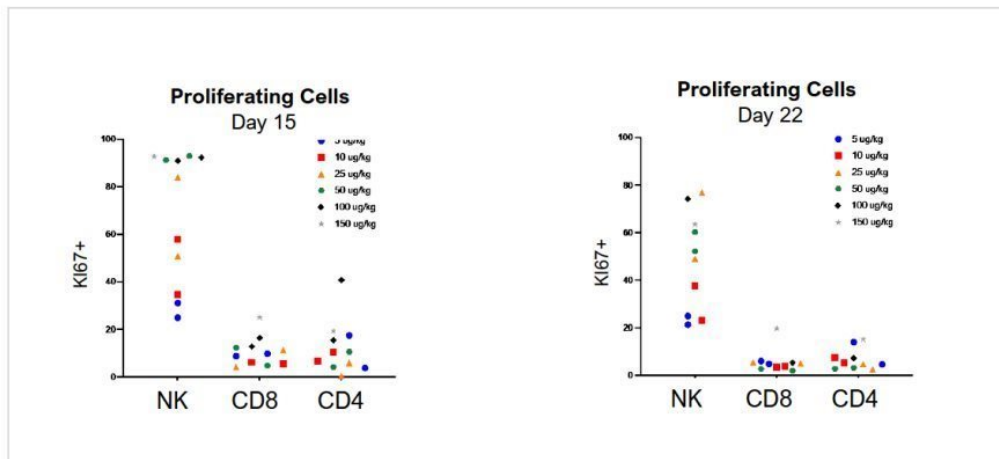


Source: Data on File, GT Biopharma, Inc.; Data cut: OnCore database July 26, 2021

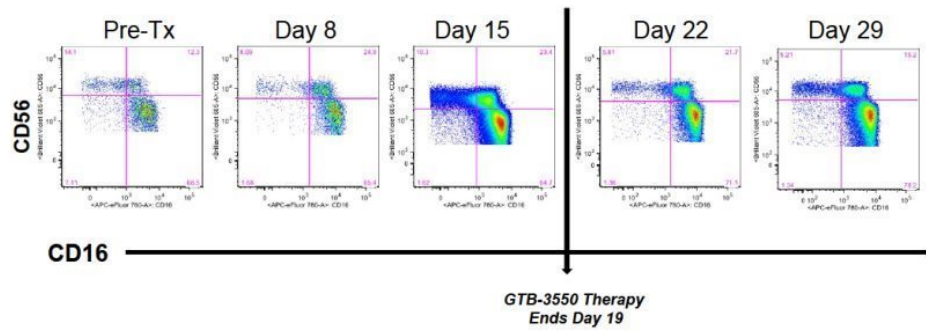
NK Cell Activation Upon Administration of GTB-3550



GTB-3550 – Sustained Proliferation of NK Cells Without Sustained Stimulation of T Cells (CD4, CD8)



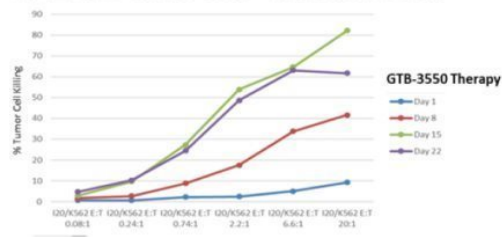
GTB-3550 – No Loss of CD16 During Treatment



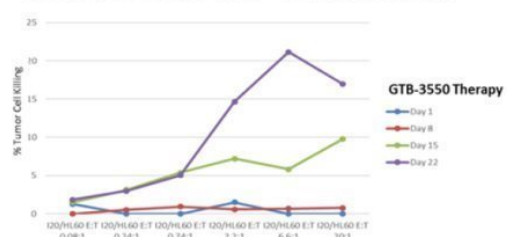
Data from Patient #11 treated with 150 µg/kg/day

GTB-3550 Rescues NK Cells and Increases Cancer Cell Killing

K562 AML Cancer Cells + Patient's NK Cells



HL60 AML Cancer Cells + Patient's NK Cells

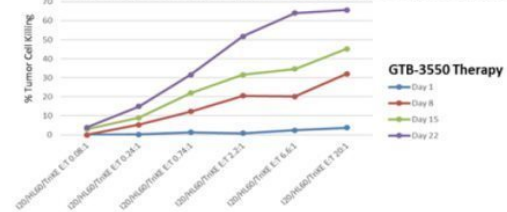


From patient #7 treated at 50 mcg/kg patient
Lysis Measured in Standard 4 hr Chromium Release

Top panels: No added cytokines or TriKE

Bottom Right: Same as Top Right but GTB-3550
(TriKE) added to the cytotoxicity assay

HL60 AML Cancer Cells + GTB-3550 + Patient's NK Cells



GTB-3550 Phase 1 Demonstrates Proof of Concept for CD33 TriKE® in AML/MDS

- GTB-3550 induces reproducible NK cell proliferation, activation and persistence in all patients at all dose levels with minimal clinically significant toxicity.
- Minimal CRS resulting from hyperactivation of patient's T-cell population at doses 5–150 µg/kg/day
 - Fever (Grade 1 CRS) observed in Subject #12 (150 µg/kg/day); resolved upon acetaminophen treatment
- No loss in CD16 expression on patient's NK cells.
- GTB-3550 significantly reduced bone marrow blast levels 33.3%, 61.7%, 63.6% in Patient 5 (25 µg/kg/day), Patient 7 (50 µg/kg/day), and Patient 9 (100 µg/kg/day), respectively
- Reduction of 50% in CD 33+ bone marrow blast levels in Patient 11 (150 µg/kg/day)
 - Patient 11 had acute biphenotypic leukemia

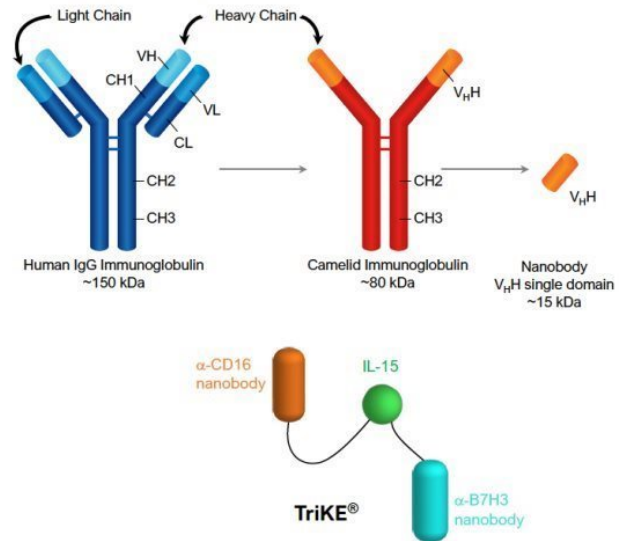


2nd Generation TriKE's

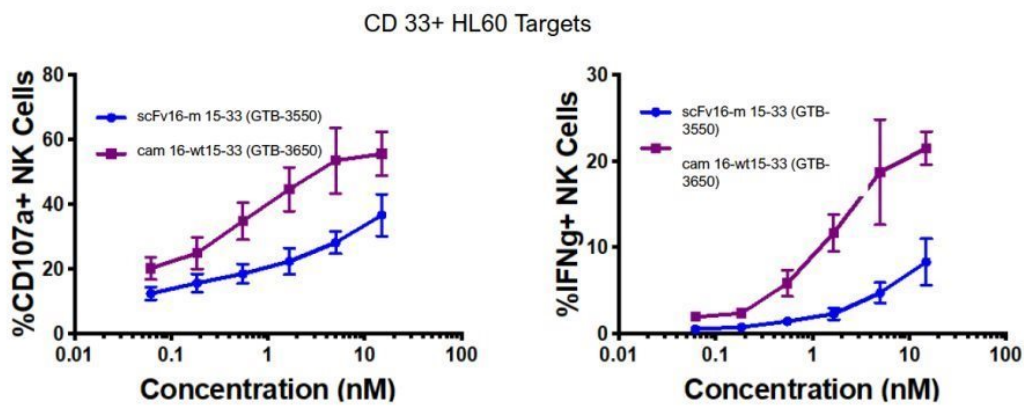
Utilize camelid nanobody technology

Advantages of Camelid Antibodies – Nanobodies in 2nd Generation TriKE's®

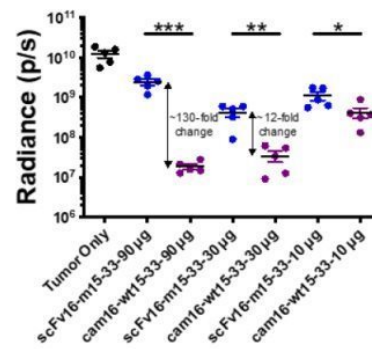
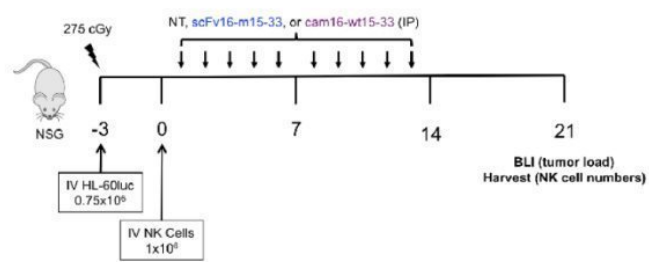
- Camelidae family of mammals include llamas, camels, and alpacas
- Camelid antibody is made up of only 2 heavy chains
 - Heavy chain IgG (hclgG)
 - Do not contain the CH1 region
 - Retain an antigen binding domain – V_HH region
- V_HH are known as single domain antibodies or nanobodies
 - Contain only the V_HH region from the camelid antibody
- 2nd Generation TriKE's utilize nanobodies
- Advantages over 1st Generation TriKE's (GTB-3550) include:
 - Improved potency and enhanced binding affinity
 - Commercial manufacturing capabilities through Cytovance
 - Proprietary molecule wholly owned by GT Biopharma
 - Similar preclinical safety profile



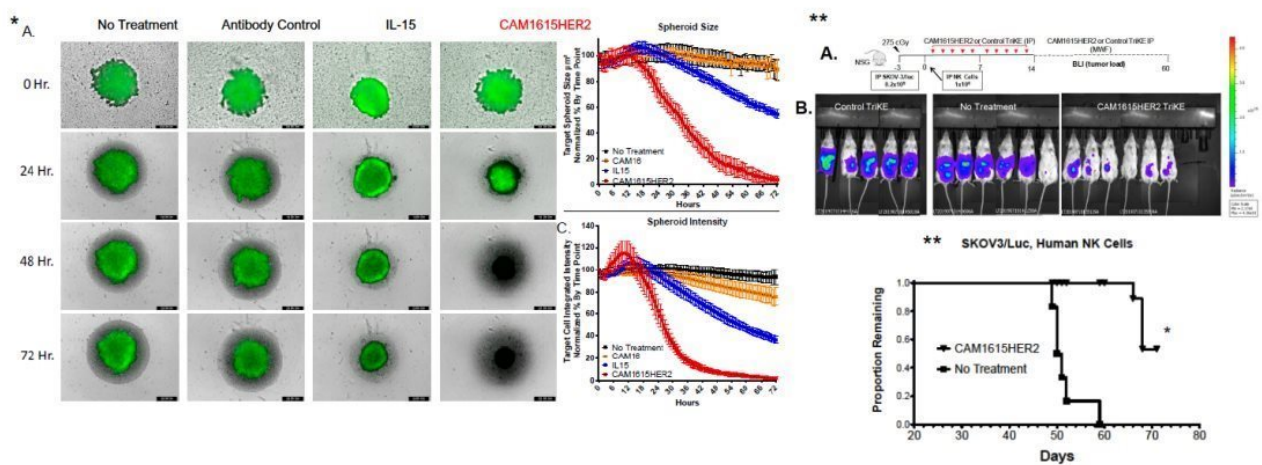
Second Generation TriKE® (Camelid) Improves NK Function



Second Generation TriKE® (Camelid) Superior In-Vivo

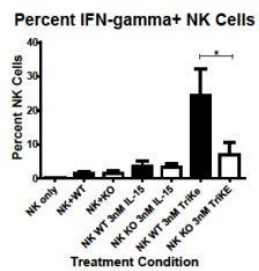
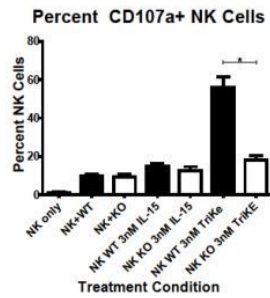
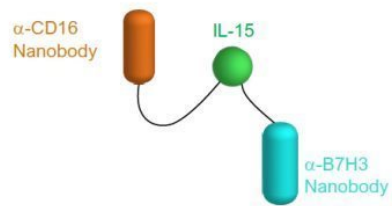


Second Generation TriKE® (Camelid) Highly Effective Against HER2+ Tumors

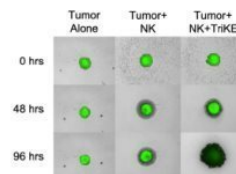
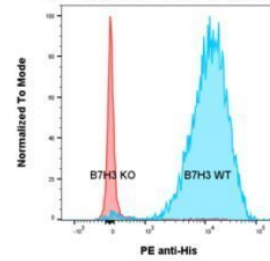


GTB 5550 – Cam1615 B7H3 TriKE® Pan Solid Tumor Targeting

GTB 5550 – Targets B7H3



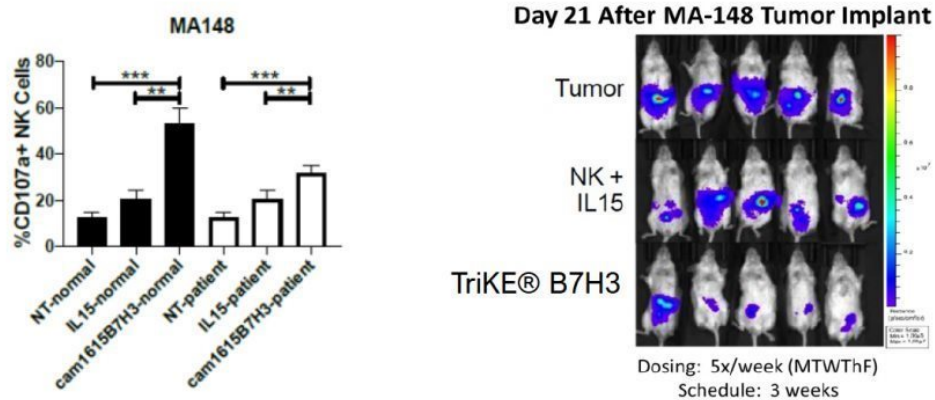
BT-12 (Atypical Teratoid/Rhabdoid)



IncuCyte-based killing assay. 20,000 OVCAR8-GFP cells were allowed to form a spheroid over 3 days, and then 40,000 NK were added alone or with B7H3 TriKE.

Source: Miller J et al. ESMO 2021

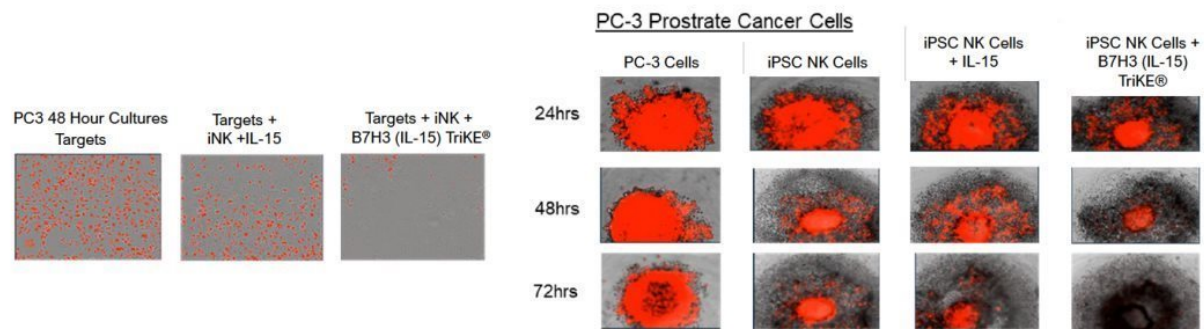
Cam1615 B7H3* TriKE® Pan Cancer Solid Tumor Targeting



Significant killing of MA148 Ovarian Cancer by TriKE® B7H3

GTB-5550 TriKE® Makes NK Cell Therapies More Effective

Competitive Advantage in Solid Tumor Cancers





Competitive Advantages

Nanobody technology, IP, and management

Competition

TriKE® Competitive Advantages

- The anti-CD16 component of the TriKE binds FcγRIII 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.

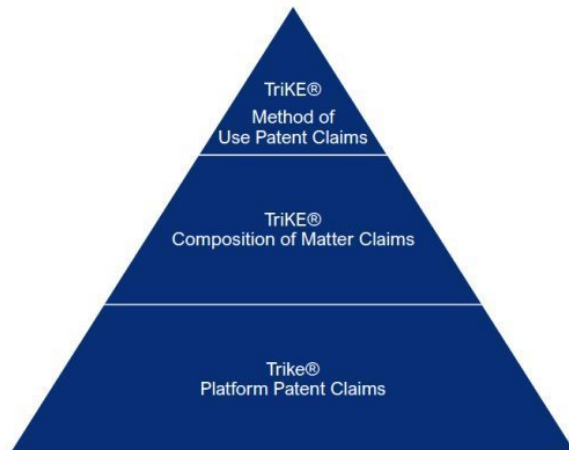


NK cell engager/antibody therapeutic strategies designed to engage CD16, NKG2D, or NKP30, but none of them co-stimulate CD16 and IL-15 simultaneously.



NK cell therapy. Significantly more expensive.

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 TME.

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

1. 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

Experienced Management Team With Deep Immuno-Oncology Experience

Proven record in biotech, pharma, product development, financing

						
Anthony Cataldo Chairman and Chief Executive Officer	Gregory Berk, MD President R&D and Chief Medical Officer	Michael Handelman, CPA Chief Financial Officer	Jeffrey Miller, MD Chief Scientific Officer, Consultant	Gavin Choy, PharmD, MBA Chief, Clinical Development Officer	Stacy Herb, MPH, MBA SVP, Portfolio Management	Leslie Bransfield, PhD VP CMC & Pharmaceutical Sciences
 	   	 		   	 	   

Investment Opportunity – Next Generation of NK Cell Engagers for Cancer

Proprietary TriKE® Platform – Camelid Nanobodies

- TriKE® platform creates tri-specific NK cells engagers targeting multiple tumor types
- Camelid “nanobodies” – now known as “third generation antibodies”
- Smallest known functional antibody fragment particularly well suited for cancer therapeutics

NK Cell Engagers – Safer than T Cells¹

- Harness the natural killing power of NK cells with protein therapeutics – NOT NK cell therapy
- Induce activation of NK cells via CD16A **and IL-15** while targeting well-known tumor antigens
- Offers a potentially safer alternative to T-cell related immunotherapy without CRS & neurotoxicity

POC Established and Broad Applicability

- GTB-3550 (targeting CD33) has now shown POC data in Phase 1 with AML patients
- GTB-3650 will supplant 3550 as 2nd generation TriKE with several advantages
- TriKE's targeting multiple tumor antigens including B7H3, HER2, CD33, PDL1

Multiple Catalysts

- 6+ pipeline assets in active preclinical development targeting both solid tumors and hematological malignancies

Well-funded Experienced Leadership

- Management team with deep expertise in all stages of oncology drug development
- Approximately \$39.5M in cash provides ample runway into 2023



*Utilizing novel camelid nanobody platform technology with
target-directed immunotherapy for cancer*

November 1, 2021
