



Tri-Specific NK Cell ENGAGERS (TriKE[®])

**Targeted NK Cell Therapies to Treat Cancer and
Autoimmune Disease**

GT Biopharma (Nasdaq: GTBP)
Corporate Presentation – November 2024

Forward Looking Statements



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, 2023, our subsequent current reports on Form 8-K, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2024, 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.

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Investment Opportunity – Next Generation of NK Cell ENGAGERS



Proprietary TriKE® Platform – Camelid Nanobodies

- TriKE® platform creates tri-specific NK cell 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 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
- IND for GTB-3650 approved in June 2024
- GTB-5550 IND submission expected H1 2025

Broad Indication Potential

- GTB-7550 TriKE® product candidate is in development for the treatment of lupus and other autoimmune disorders
- Exploring manufacturers for GTB-7550

Well-funded Experienced Leadership

- Management team with deep expertise in all stages of oncology drug development
- \$9.2M in cash + short-term investments as of June 30, 2024 (unaudited), anticipated to be sufficient to fund operations into 2025, debt free balance sheet

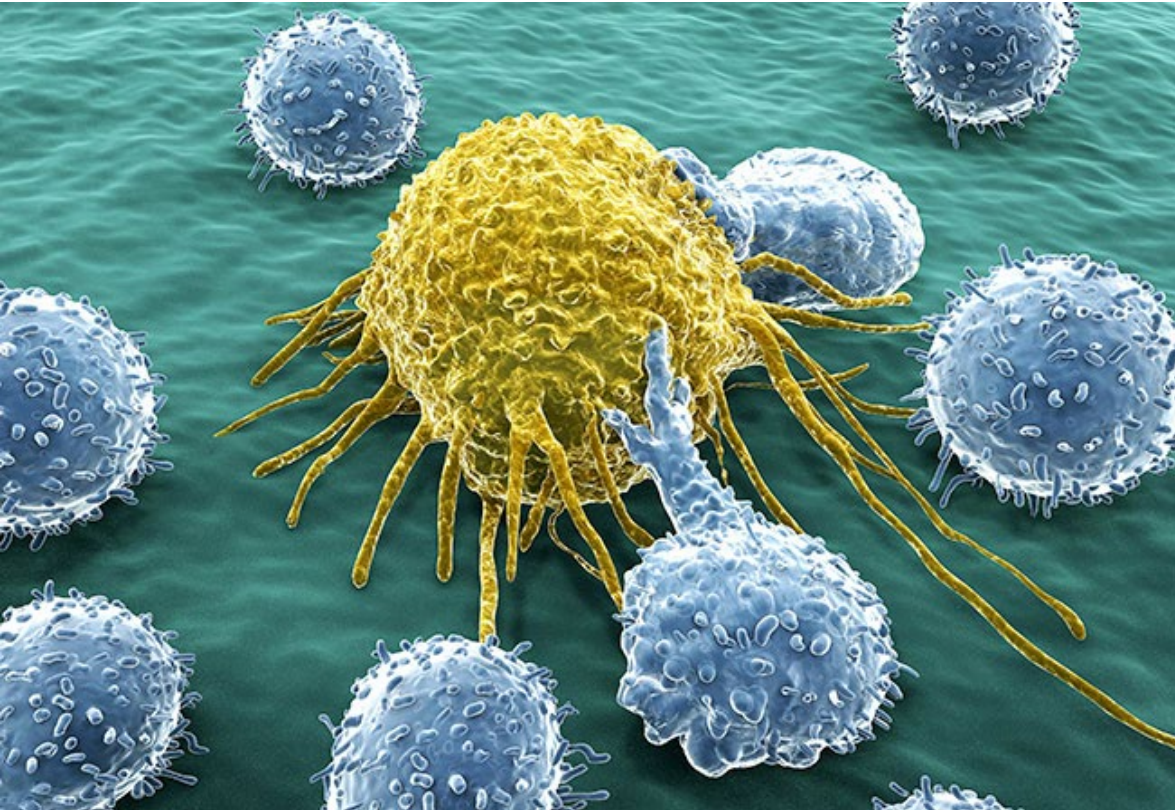
1. [Demaria](#), et.al. Eur J. of Immun; (2021)51:8; 1934

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					<div style="border: 1px solid red; padding: 5px; color: red; font-weight: bold;"> GTB-3550 supplanted by second generation nanobody GTB-3650 </div>
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					<div style="border: 1px solid red; padding: 5px; color: red; font-weight: bold;"> GTB-5550 IND submission expected H1 2025 </div>
GTB-6550	Monotherapy & Combination	HER2	Solid Tumors					
GTB-7550	Monotherapy & Combination	CD19	B-Cell Malignancies					
GTB-1050	Monotherapy & Combination		HIV					
Undisclosed Candidates	Monotherapy & Combination		Solid & Hematological Malignancies					

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

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

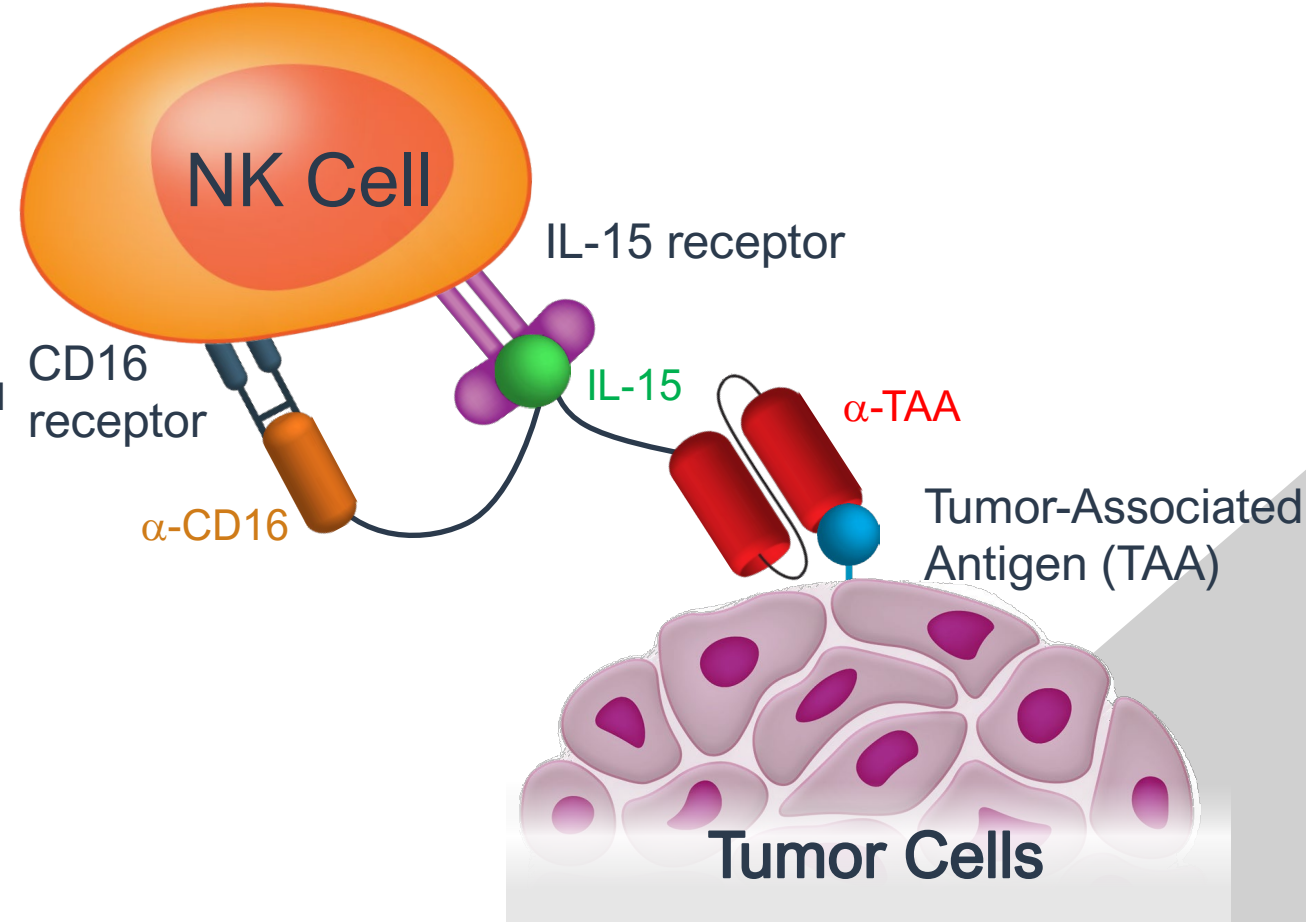
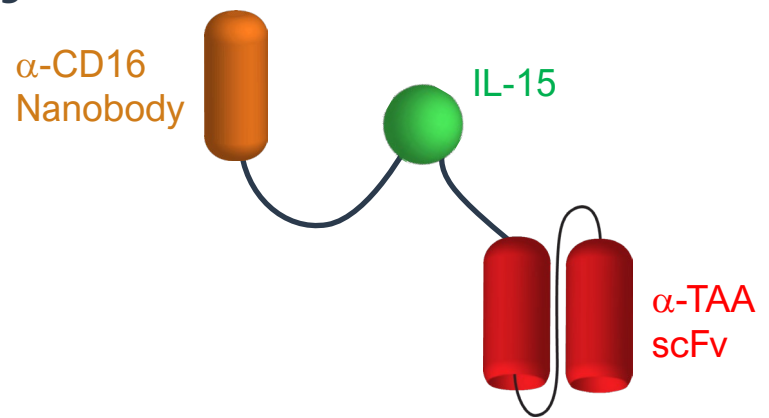
www.dana-farber.org/newsroom/publications/paths-of-progress-2019/natural-killer-cells/

TriKE[®]: Tri-Specific Natural Killer (NK) Cell ENGAGERS - A 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

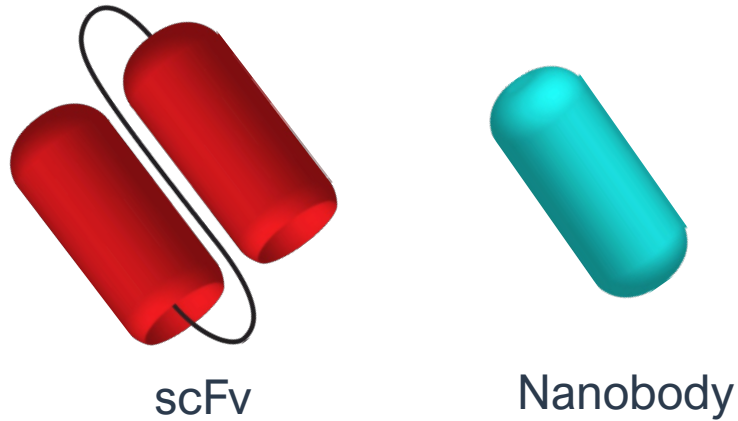


* 1st generation TriKE GTB3550 utilizes scFv for a-CD16 1. [Semin Immunol. 2017 Jun; 31: 64–75.](#)

2. [J Exp Med. 1994 Oct 1; 180\(4\): 1395–1403.](#)

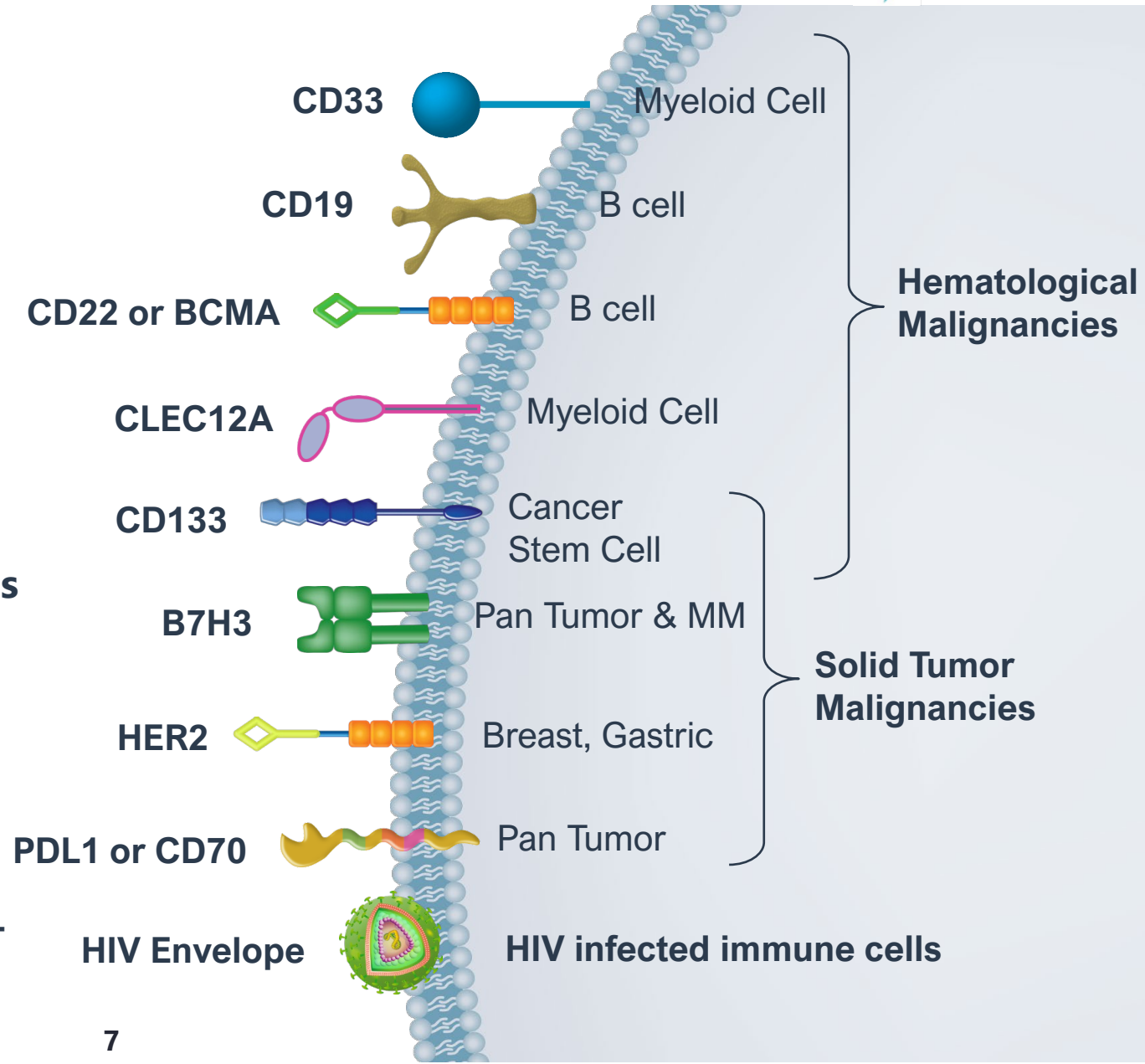
3. [Vallera et. al. Clin Cancer Res. 22\(14\) July 15, 2016](#)

TriKE® Modular Platform Allows for Multiple Tumor-Associated Antigen



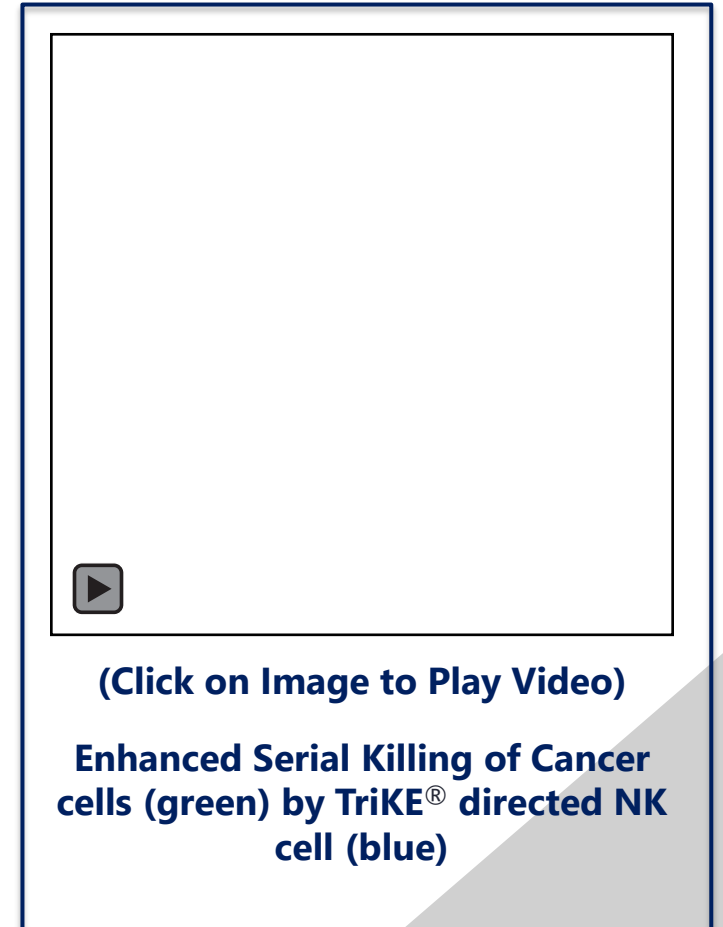
Anti-Tumor Associated Antigen

- 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**



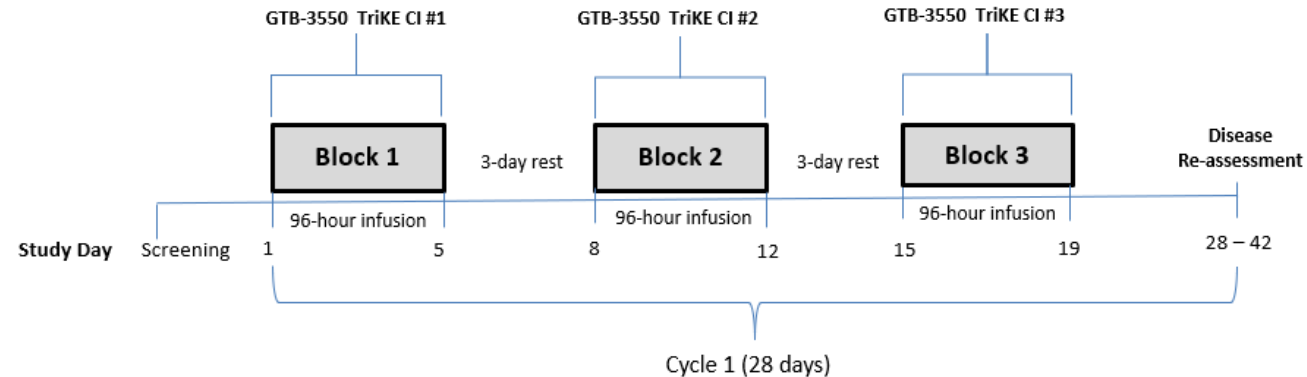
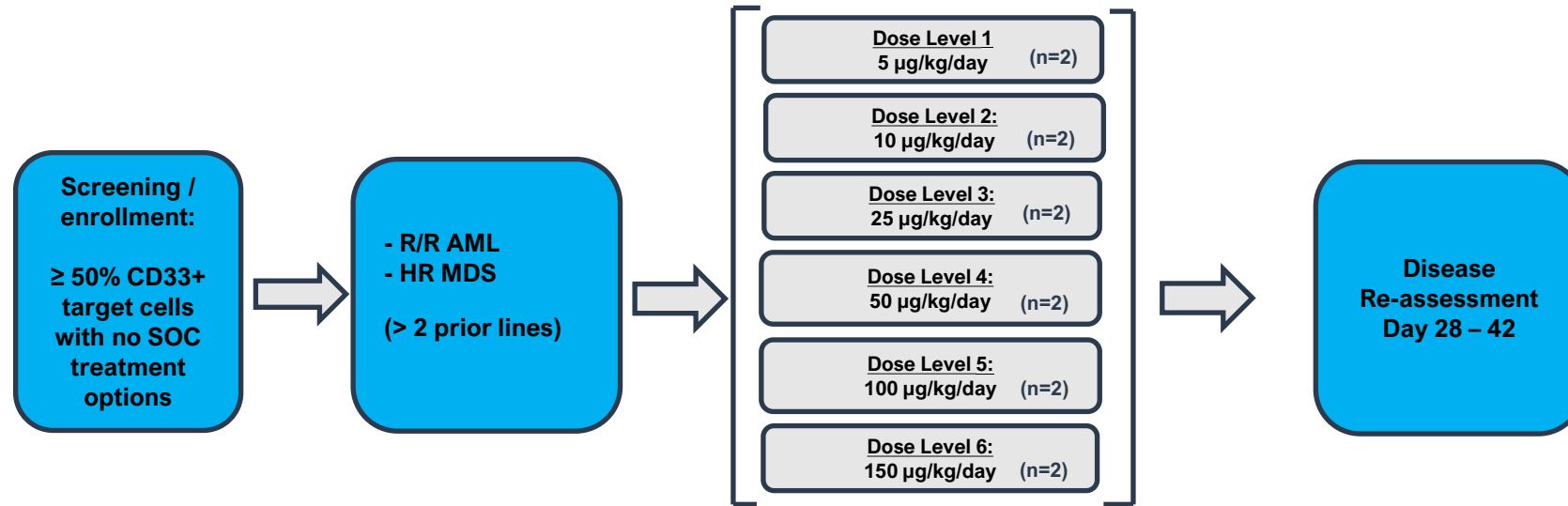
Source: [Sarhan D et al. Blood Adv 2018 Jun 26; 2\(12\): 1459–1469](#)



GTB 3550 for AML and MDS

First generation TriKE® provides POC for platform

GTB-3550 AML/MDS Phase 1 Study Design

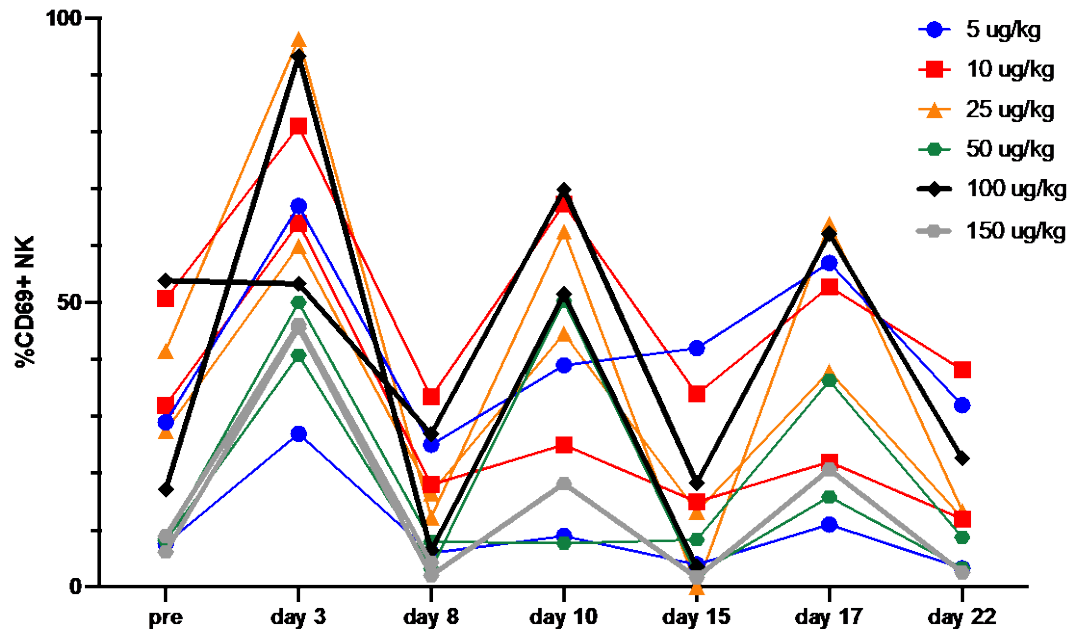


Phase 1 (safety and dose finding)

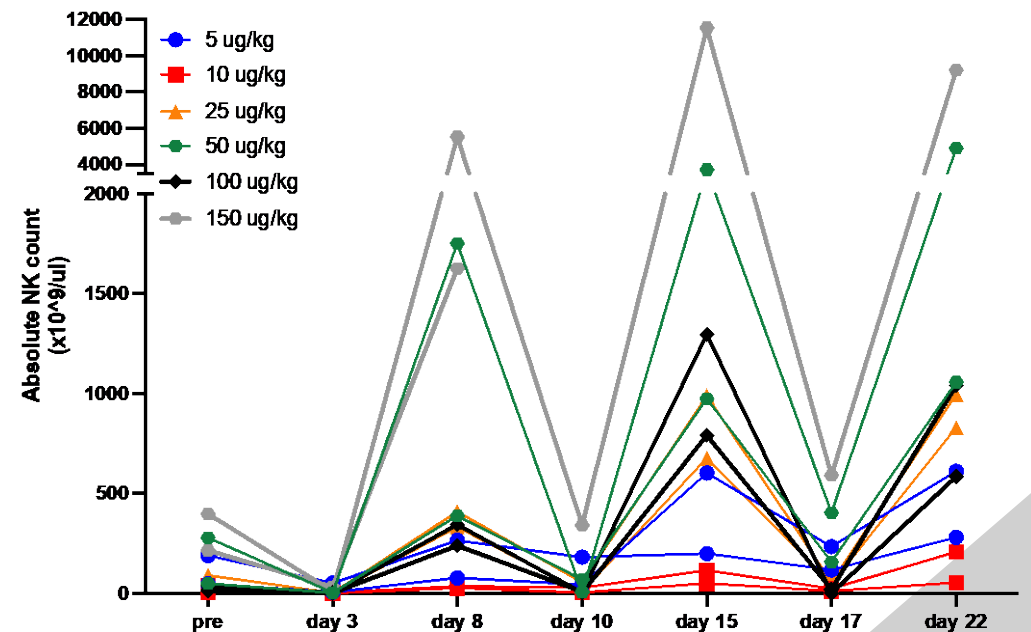
- Six dose levels
- Escalation based on continual reassessment method; Cohorts of 2 subjects
- Day 28 (end of DLT assessment period)

GTB-3550 Activation of Endogenous NK Cells

Panel A: Increase in NK cell activation upon administration of GTB-3550 (n= 2 patients per dose)



Panel B: Increase in absolute number of NK cells during treatment (n= 2 patients per dose)



Source: Data on File, GT Biopharma, Inc.

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. 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 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

- **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 CD 33+ bone marrow blast levels by 33.3%, 61.7%, 63.6%, 50% 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**
- **After the end of infusion, GTB-3550 & IL-15 concentrations declined rapidly with overall geometric mean terminal phase elimination half-life (T1/2) of 2.2 and 2.52 hours, respectively**



GT BIOPHARMA

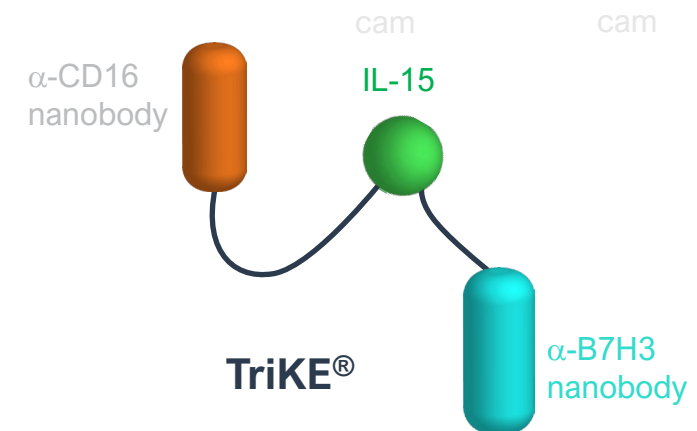
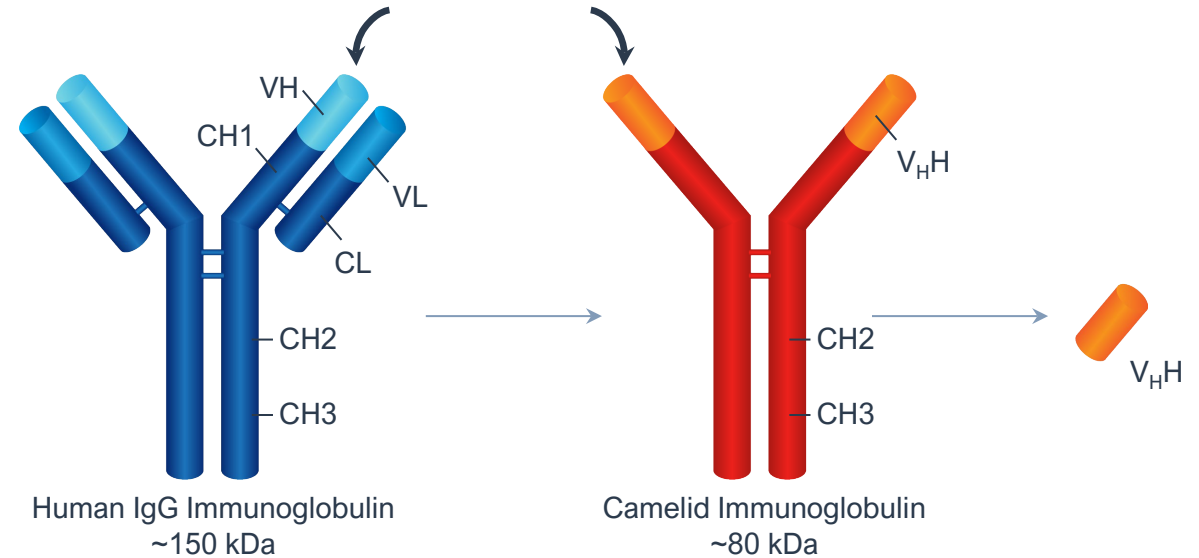
**GTB 3650 for AML and MDS
GTB 5550 for Solid Tumors**

**Second generation TriKEs® utilize
camelid nanobody technology**

Advantages of Camelid Antibodies – Nanobodies in 2nd Generation TriKEs®

- 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

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

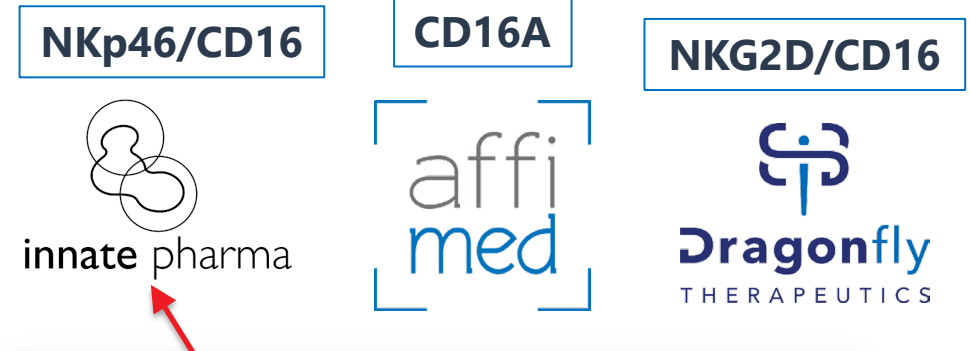


Advantage – Simultaneous Co-Stimulation of CD16 and IL-15



TriKE[®] Competitive Differentiation

- The anti-CD16 component of the TriKE[®] binds FcRγIII with high affinity compared to ADCC mediated strategies that bind with low affinity
- TriKE[®] 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
- IL-15 in TriKE[®] is less active surrounded by ENGAGERS than rhIL-15 that induces exhaustion
- TriKE[®] can be targeted to heme malignancies, solid tumors and infectious diseases



- NK cell ENGAGER/antibody therapeutic strategies designed to engage CD16, NKG2D, or NKp30
- None of them co-stimulate CD16 and IL-15 simultaneously

CD123 in AML



- NK cell therapy
- Significantly more expensive
- Could be used in combination with TriKE[®]s



GT BIOPHARMA

GTB 7550 for Autoimmune Disease

Targeting CD19 for B-Cell Depletion In Vivo

GTB 7550 for Autoimmune Disease

- **GTB-7550 TriKE[®] product candidate is in development for the treatment of lupus and other autoimmune disorders**
- **GTB-7550 TriKE[®] is a tri-specific molecule composed of a camelid nanobody that binds the CD16 receptor on NK cells, a scFv ENGAGER against CD19 on malignant and normal B cells, and a human IL-15 sequence between them**
- **Published data shows that GTB-7550 effectively targets CD19+ malignant cell lines and primary chronic lymphocytic leukemia (CLL)**
- **Preliminary data shows that GTB-7550 can target and eliminate normal B cells**
- **NSG mice will test the ability of GTB-7550 to deplete normal B cells in vivo**
- **Exploring manufacturers for GTB-7550**
- **Quickest path to clinic may be testing safety in B cell malignancy first**

GTB 7550 for Autoimmune Disease

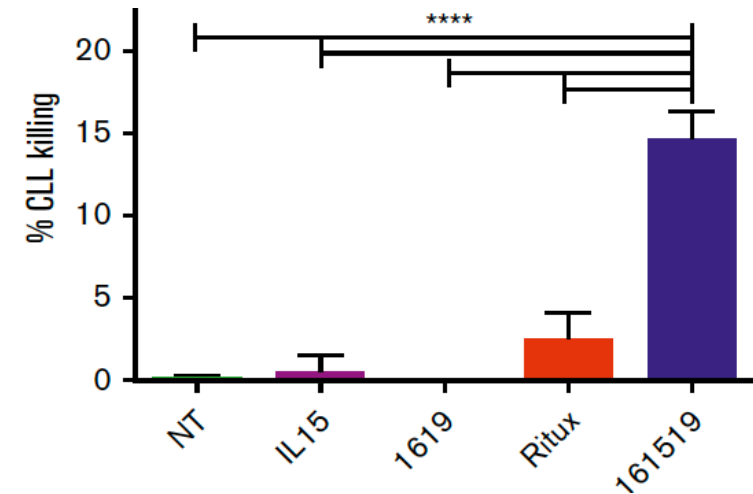
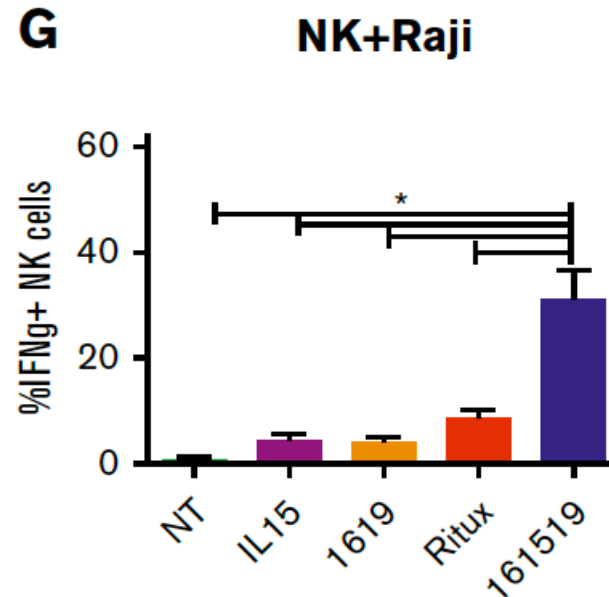
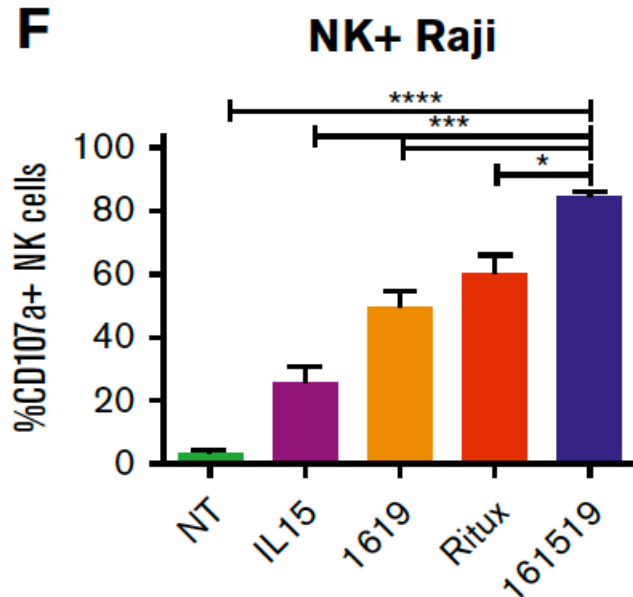
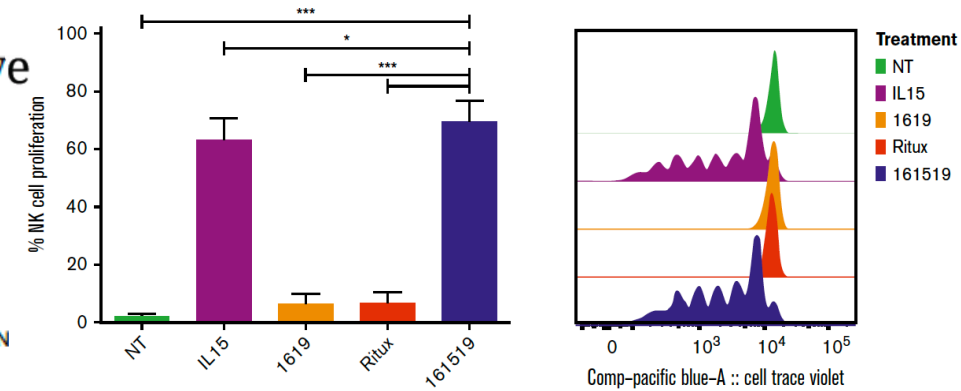
REGULAR ARTICLE

blood advances

Novel CD19-targeted TriKE restores NK cell function and proliferative capacity in CLL

Martin Felices,¹ Behiye Kodal,¹ Peter Hinderlie,¹ Michael F. Kaminski,¹ Sarah Cooley,¹ Daniel J. Weisdorf,¹ Daniel A. Vallera,² Jeffrey S. Miller,¹ and Veronika Bachanova¹

¹Division of Hematology, Oncology, and Transplantation, Department of Medicine, and ²Department of Radiation Oncology, University of Minnesota, Minneapolis, MN



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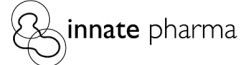





For more information, please visit: www.gtbiopharma.com



APPENDIX



Recent M&A and BD Deals Highlight Value of NK Cell ENGAGERS and Immuno-Oncology

Innovator					
Acquirer					
Date	8/27/2018	11/9/2020	12/21/2021	5/2/2022	12/19/22
Deal Type	License Deal	Single Molecule Preclinical License Deal	Company Acquisition	Single Molecule Preclinical License Deal	Collaboration Expansion License Deal
Key Deal Terms	<ul style="list-style-type: none"> • \$96M upfront • \$5B in additional milestones 	<ul style="list-style-type: none"> • \$60M upfront • \$2B in milestones 	<ul style="list-style-type: none"> • \$1 billion upfront • \$225M in milestones 	<ul style="list-style-type: none"> • \$300M cash upfront • Undisclosed milestones • 20% royalties 	<ul style="list-style-type: none"> • €25M upfront • €1.3B in milestones • Royalties
Technology / Mechanism	Redirected Optimized Cell Killing (ROCK®) platform to generate both NK cell and T cell-engaging antibodies	ROCK® platform generates tetravalent, bispecific antibodies as innate cell ENGAGERS (ICE®) customized to target specific domains on hematologic and solid tumor cells	<ul style="list-style-type: none"> • Portfolio of T cell ENGAGERS using XTEN technology • Lead asset AMX-818 in pre-clinicals 	<ul style="list-style-type: none"> • NK-cell ENGAGER • DF7001 is a TriNKET designed to activate and direct NK and cytotoxic T cell killing of cancer cells 	<ul style="list-style-type: none"> • NK cell ENGAGER • Targeting B7H3 • ANKET™ platform • Option to add 2 additional targets
Rationale	Allowed Roche access to Affimed platform to explore range of ENGAGER constructs for multiple oncology applications	Grants Roivant a license to the preclinical molecule AFM32	Combine Amunix's complementary molecules with Sanofi's immuno-oncology portfolio	Enhance Gilead's portfolio with complementary MOAs and scientific rationale for combination opportunities	Allogeneic NK cell immunotherapy is pillar of Sanofi's overall oncology strategy and using engineered lymphokines to stimulate NK cells is a key component

Experienced Team With Deep Immuno-Oncology Experience



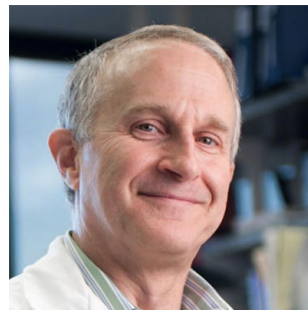
Proven Record in Biotech, Pharma, Product Development, Financing



Michael Breen, LL.B
Executive Chairman and
Interim Chief Executive Officer



Alan Urban
Chief Financial Officer
CPA (Inactive)



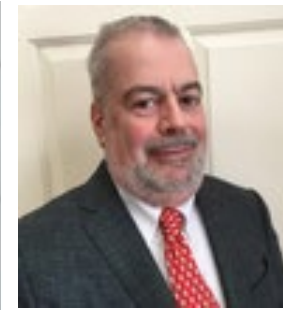
Jeffrey Miller, MD
Consulting Senior
Medical Director ¹



Martin Felices, PhD
Consulting Scientist



Chris Hendry
Consultant, CMC and
Pharmaceutical Science



Bruce Wendel
Board of Directors
Compensation Committee
Chair



Rajesh Shrotriya, MD
Board of Directors
Nominating and Corp. Gov.
Committee Chair



Charles J Casamento
Board of Directors
Audit Committee Chair



The University of Minnesota, pursuant to its license agreement with GT Biopharma, is entitled to receive royalties should commercial sales of GTB-3650 be realized. This interest has been reviewed and managed by the University of Minnesota in accordance with its conflict of interest policies.



1. Dr. Miller is the Consulting Senior Medical Director at GT Biopharma and holds stock and options in GTBP.

Selected Financial Information

ASSETS	UNAUDITED AS OF SEPT 30, 2024	AUDITED AS OF DEC 31, 2023
Cash + Short Term Investments	\$ 6,511,000	\$ 13,972,000
Other Assets	<u>248,000</u>	<u>137,000</u>
Total Assets	6,759,000	14,109,000
LIABILITIES		
Accounts Payable + Accrued Expenses	\$ 4,480,000	\$ 5,523,000
Other Liabilities	-	58,000
Warrant Liability	<u>182,000</u>	<u>1,052,000</u>
Total Liabilities	4,662,000	6,633,000
STOCKHOLDERS' EQUITY		
Total Stockholders' Equity	\$ 2,097,000	\$ 7,476,000

Capitalization Table

SECURITY	AS OF SEPT 30, 2024	WEIGHTED AVERAGE EXERCISE PRICE	PERCENTAGE FULLY DILUTED
Common Stock Outstanding	2,234,328	N/A	64%
Legacy Warrants	304,962	\$64.32	9%
2024 Warrants	828,800	\$4.47	24%
Stock Options	<u>101,264</u>	\$39.74	<u>3%</u>
Fully Diluted Shares	3,469,354		100%
MAJOR SHAREHOLDERS	AS OF SEPT 30, 2024	SECURITY	PERCENTAGE OF COMMON STOCK OUTSTANDING
Cytovance Biologics, Inc.	219,457	Common Stock	9.8%
Bristol Investment Fund, Ltd. ¹	190,000	Common Stock	8.5%

¹ Per ownership disclosure filed May 23, 2024