# Tri-Specific NK Cell ENGAGERS (TriKE®)

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

GT Biopharma (Nasdaq: GTBP)

Corporate Presentation – June 2025

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# Investment Opportunity – Next Generation of NK Cell ENGAGERS

| | |
|---|---|
| **Proprietary TriKE® Platform – Camelid Nanobodies** | • TriKE® are tri-specific NK cell ENGAGERS<br>• Incorporate Camelid "nanobodies" |
| **NK Cell ENGAGERS – Safer than T Cells[1]** | • Protein therapeutics to harness the natural killing power of NK cells with – NOT NK cell therapy<br>• Activates NK cells via CD16A and IL-15 while targeting tumor antigens<br>• Potentially safer than T-cell immunotherapy |
| **POC Established and Broad Applicability** | • GTB-3550 (targeting CD33) showed POC in Phase 1 in AML patients<br>• GTB-3650 will supplant 3550 as 2nd generation TriKE® with several advantages<br>• TriKE®s target multiple tumor antigens including B7H3, HER2, CD33, PDL1 |
| **Multiple Catalysts** | • 6+ pipeline assets in preclinical development, both solid tumors and hematological malignancies<br>• IND for GTB-3650 accepted in June 2024, first patient dosed on Jan 21, 2025 |
| **Broad Indication Potential** | • GTB-7550 TriKE® candidate in development for the treatment of lupus, other autoimmune disorders<br>• Exploring manufacturers for GTB-7550 |
| **Well-funded Experienced Leadership** | • Management team with deep expertise in all stages of oncology drug development<br>• $2.5M in cash + short-term investments as of March 31, 2025, debt free balance sheet<br>• Additional $5.4M in cash raised on May 12, 2025 |

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

# TriKE® Pipeline

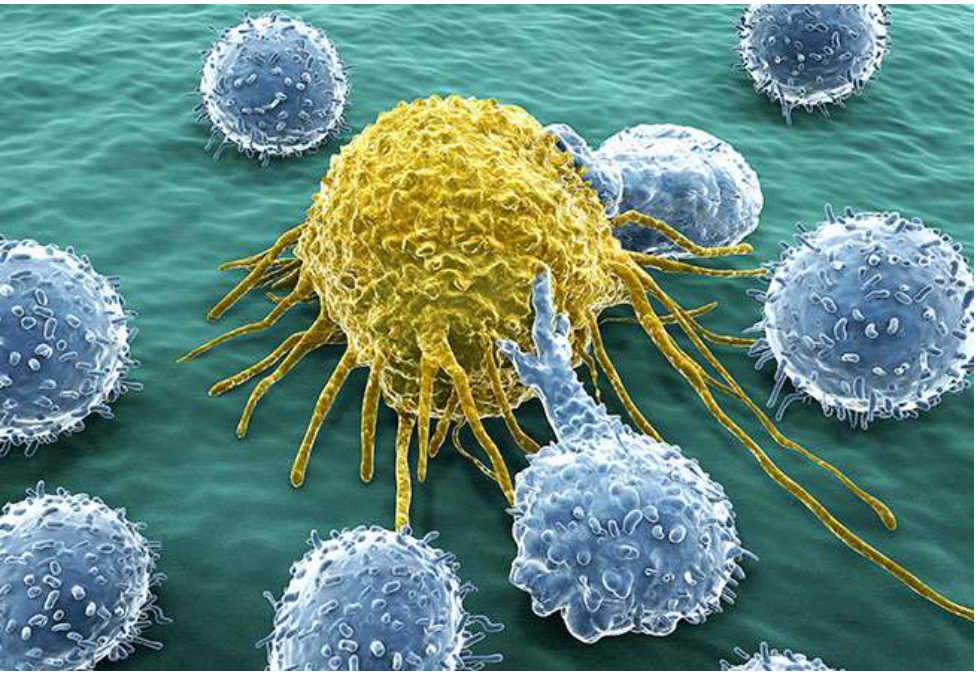
| TriKE® Product Candidates | Approach | Target | Indication | Pre-Clinical | IND-Enabling/ GMP Manufacturing | Phase 1 | Phase 2 |
|---|---|---|---|---|---|---|---|
| **GTB-3650 2nd Generation Camelid** | Monotherapy | CD33 | Leukemia – AML, MDS | | | | |
| | Combination with Chemotherapy | CD33 | Leukemia – AML, MDS | | | | |
| **GTB-5550** | Monotherapy & Combination | B7H3 | Solid Tumors | | | | |
| **GTB-6550** | Monotherapy & Combination | HER2 | Solid Tumors | | | | |
| **GTB-7550** | Monotherapy & Combination | CD19 | B-Cell Malignancies | | | | |
| **GTB-1050** | Monotherapy & Combination | | HIV | | | | |
| **Undisclosed Candidates** | Monotherapy & Combination | | Solid & Hematological Malignancies | | | | |
| ***GTB-3550*** | *Monotherapy* | *CD33* | *Leukemia – AML, MDS* | | | | |

**GTB-3650 Phase 1 trial initiated: First patient dosed on 01/21/2025**

***GTB-3550 supplanted by second generation GTB-3650***

**Clinical Product Candidates** **Preclinical Product Candidates** **Development Abandoned**

# 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**

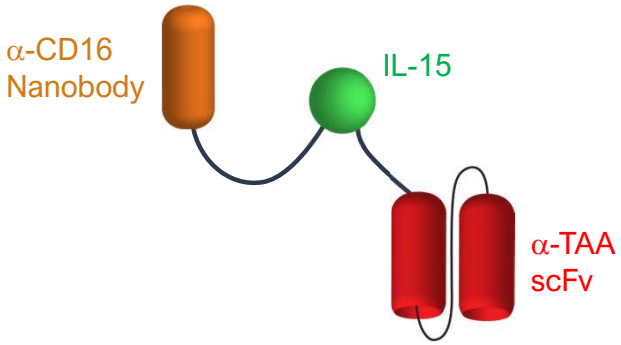
**www.dana-farber.org/newsroom/publications/paths-of-progress-2019/natural-killer-cells/**

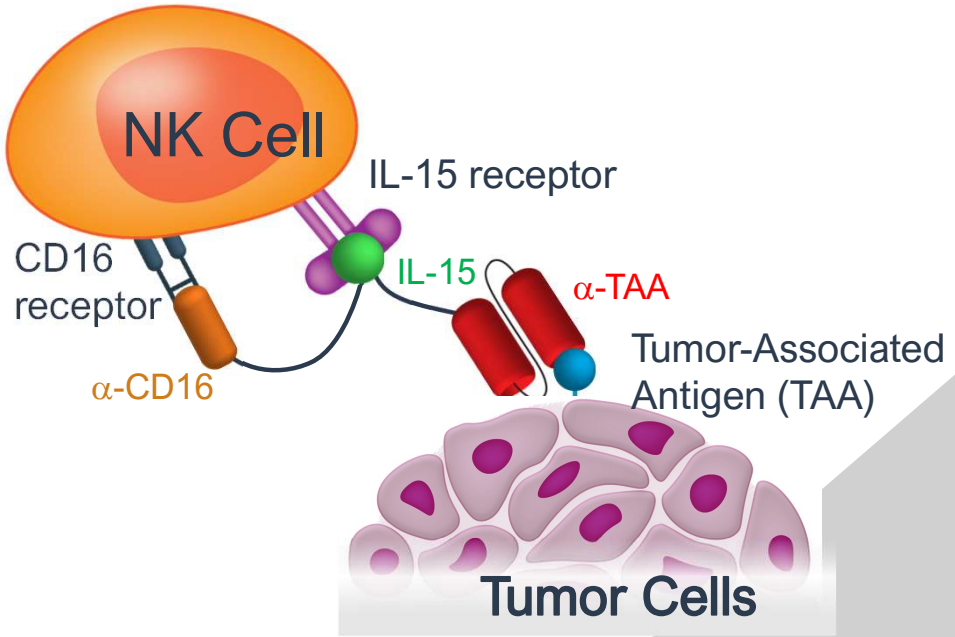
# TriKE®: Tri-Specific Natural Killer (NK) Cell ENGAGERS - A Modular Platform

**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**



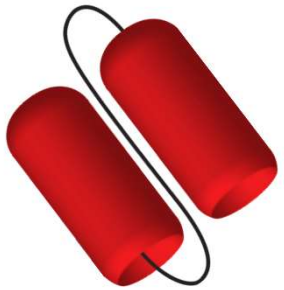

* 1st generation TriKE GTB3550 utilizes scFv for a-CD16

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

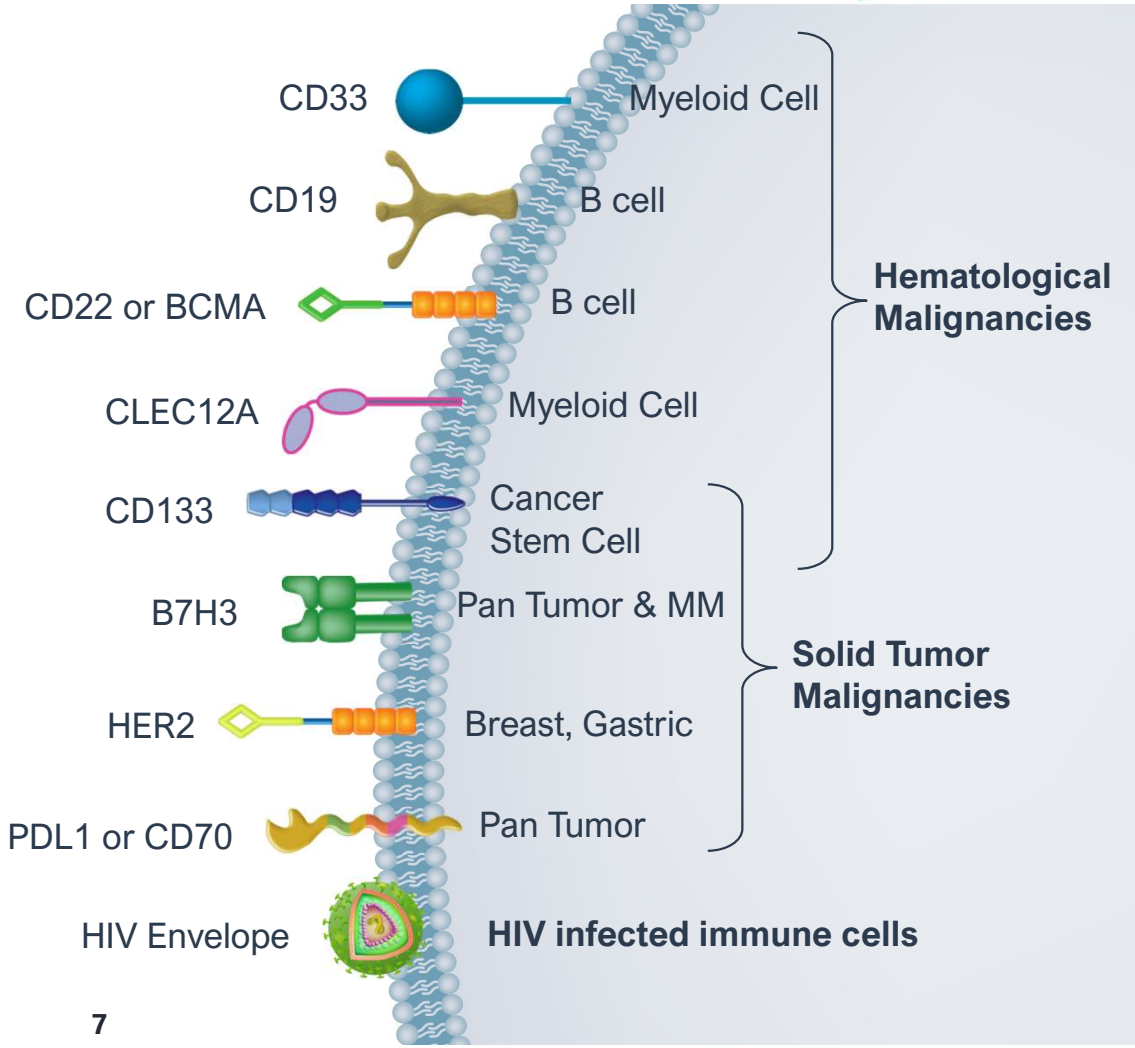


scFv

Nanobody

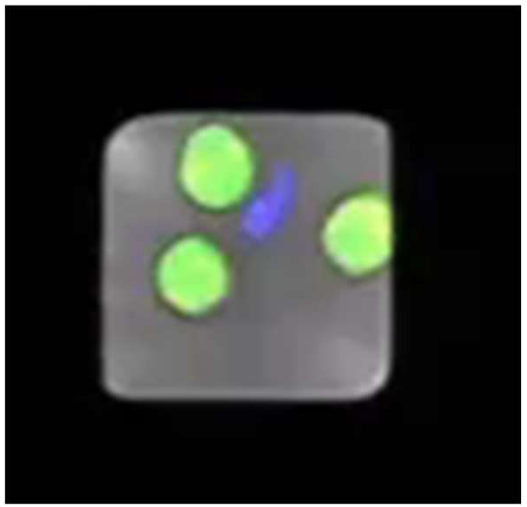
## Anti-Tumor Associated Antigen

- 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



**(Click on Image to Play Video)**

**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**

## 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 acetominophen 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

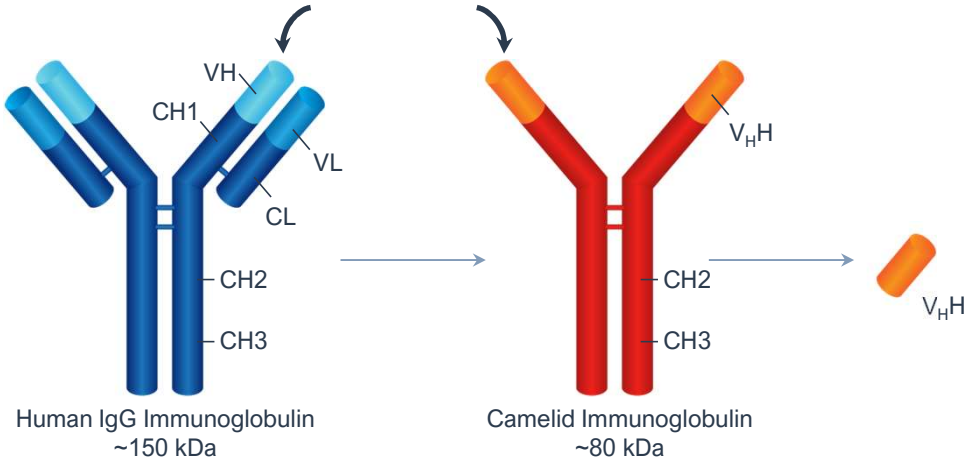
GT BIOPHARMA

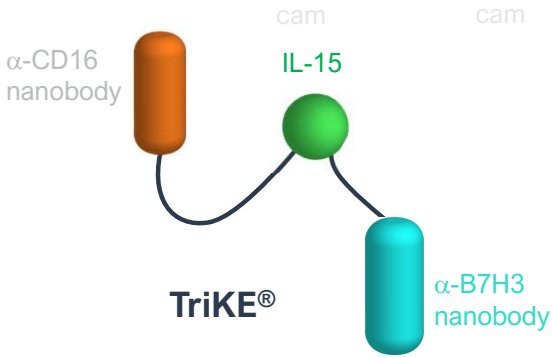
# GTB 3650 for AML and MDS
# GTB 5550 for Solid Tumors

**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 (hcIgG)
  - 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



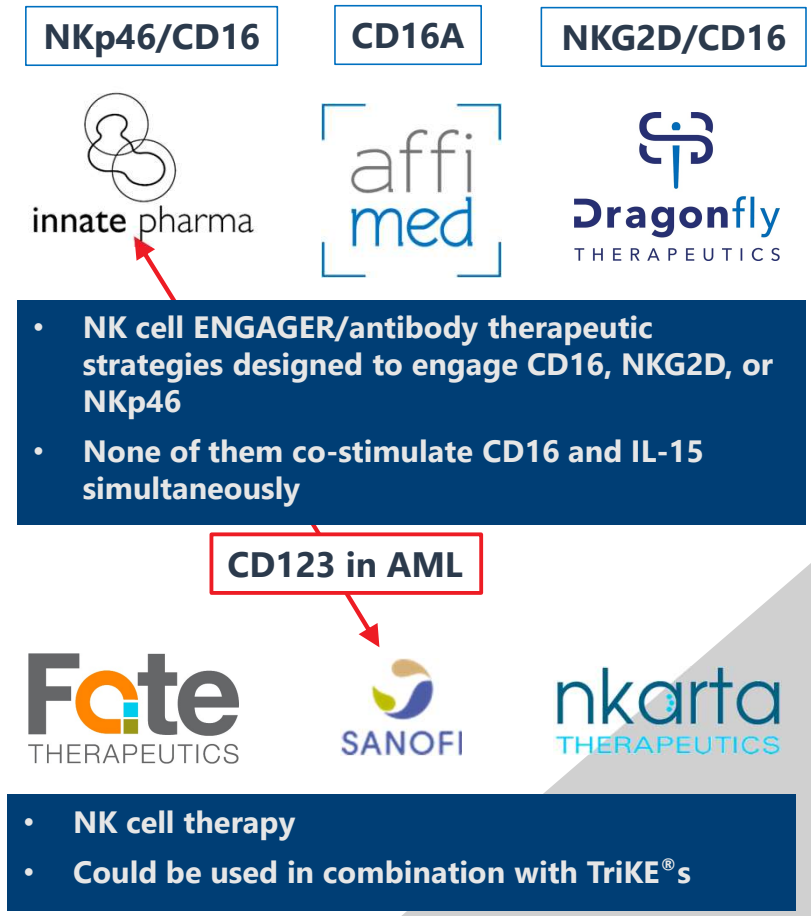




Source: www.rndsystems.com/products/llamabody-camelid-antibodies

# Our Approach – Co-Stimulation of CD16 and IL-15

## TriKE® Competitive Differentiation

- The anti-CD16 component of the TriKE® binds FcRγIII with high affinity
- TriKE® does not result in proliferation of T-cells
- IL-15 provides NK cell specific proliferation with less bystander T-cell activity compared to the IL-15 protein itself
- IL-15 in TriKE® is less active surrounded by ENGAGERS than rhIL-15
- TriKE® can be targeted to heme malignancies, solid tumors and infectious diseases



# 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 be used to 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

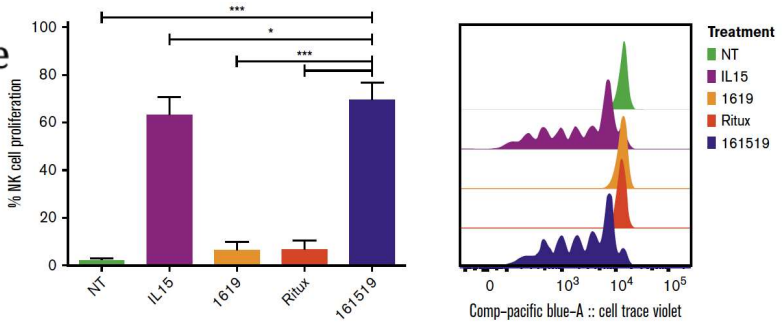
REGULAR ARTICLE

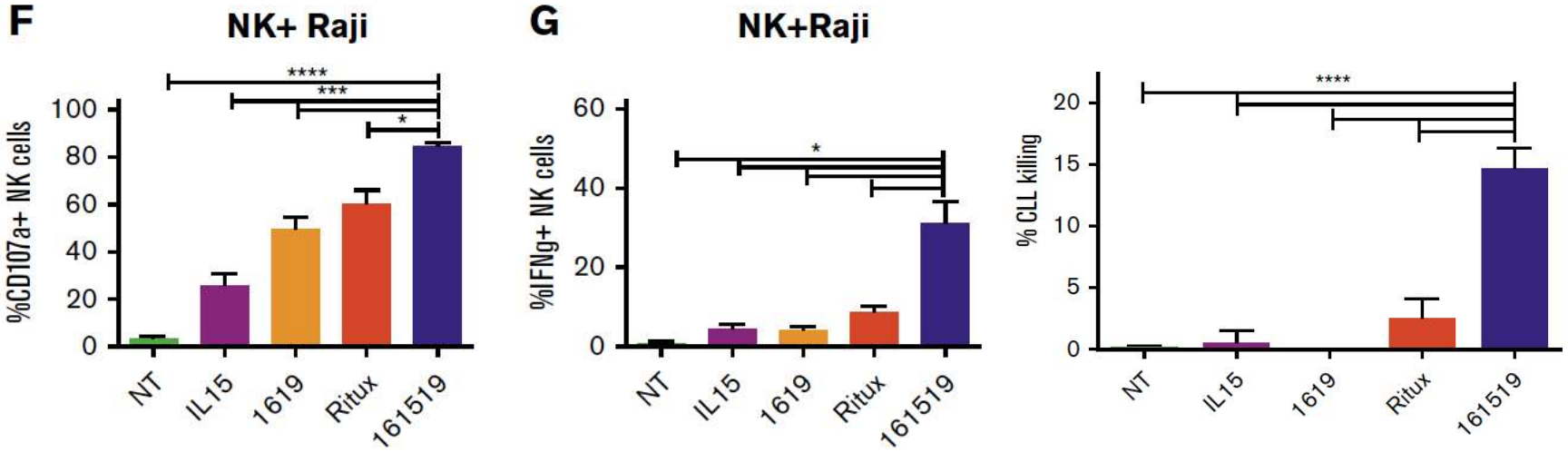
blood advances

## 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 Bachanova[1]

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



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

# Contact Us


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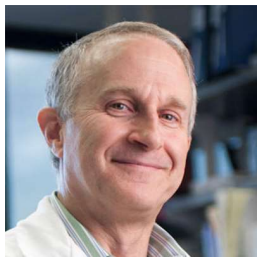
# APPENDIX

# Experienced Team With Deep Immuno-Oncology Experience

## Proven Record in Biotech, Pharma, Product Development, Financing

**Michael Breen, LL.B**
Executive Chairman and 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

**Hilary Kramer**
Board of Directors
Nominating and Corp. Gov. Committee Chair

**David C. Mun-Gavin**
Board of Directors
Compensation Committee Chair

**Charles J Casamento**
Board of Directors
Audit Committee Chair

BNP PARIBAS
INSINGER de BEAUFORT
CLYDE&CO
Research Solutions
infotrieve
REACHLOCAL
UNIVERSITY OF MINNESOTA
UNIVERSITY OF MINNESOTA

**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.**

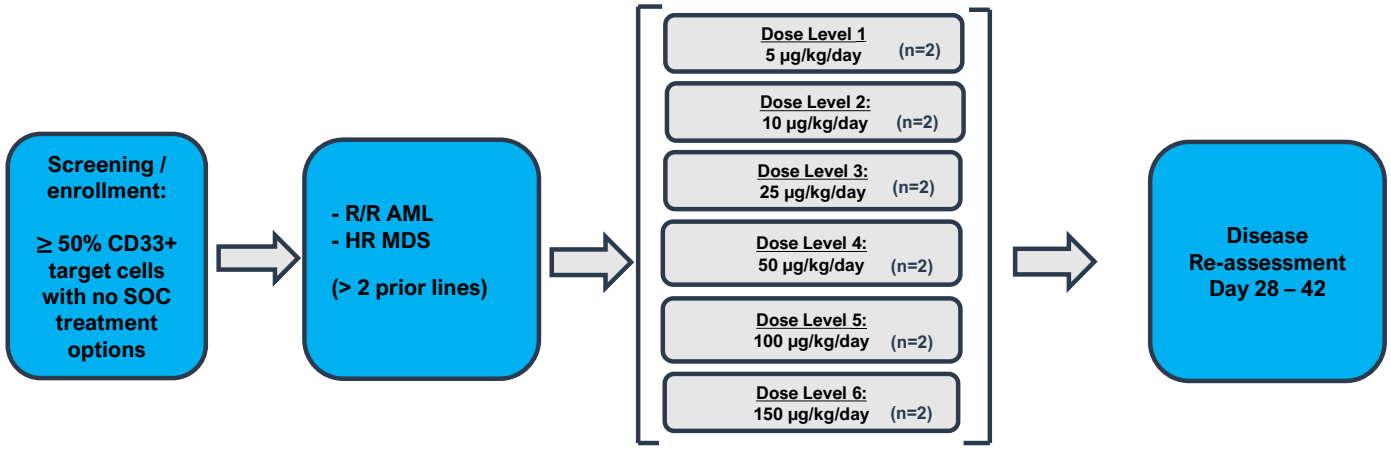
STC Biologics
Allena PHARMACEUTICALS
seragen
Morgan Stanley
LEHMAN BROTHERS
DIRECTV
BROWN SHIPLEY
A QUINTET PRIVATE BANK
CREDIT SUISSE
INSINGER de BEAUFORT
Indevus Pharmaceuticals, Inc.
SANOFI GENZYME

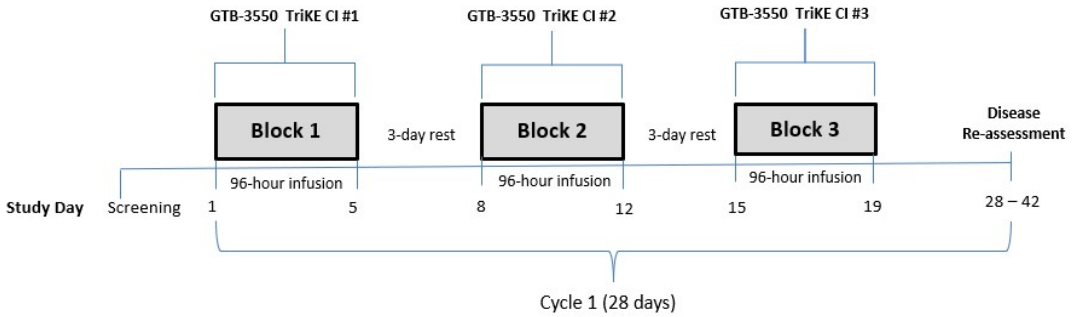
1. **Dr. Miller is the Consulting Senior Medical Director at GT Biopharma and holds stock and options in GTBP.**

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

| Innovator | AFFIMED | AFFIMED | AMUNIX | Dragonfly | innate pharma |
|---|---|---|---|---|---|
| **Acquirer** | SANOFI | ROIVANT SCIENCES | SANOFI | GILEAD | SANOFI |
| **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** | • $96M upfront<br>• $5B in additional milestones | • $60M upfront<br>• $2B in milestones | • $1 billion upfront<br>• $225M in milestones | • $300M cash upfront<br>• Undisclosed milestones<br>• 20% royalties | • €25M upfront<br>• €1.3B in milestones<br>• 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 | • Portfolio of T cell ENGAGERS using XTEN technology<br>• Lead asset AMX-818 in pre-clinicals | • NK-cell ENGAGER<br>• DF7001 is a TriNKET designed to activate and direct NK and cytotoxic T cell killing of cancer cells | • NK cell ENGAGER<br>• Targeting B7H3<br>• ANKET™ platform<br>• 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 |

# GTB-3550 AML/MDS Phase 1 Study Design



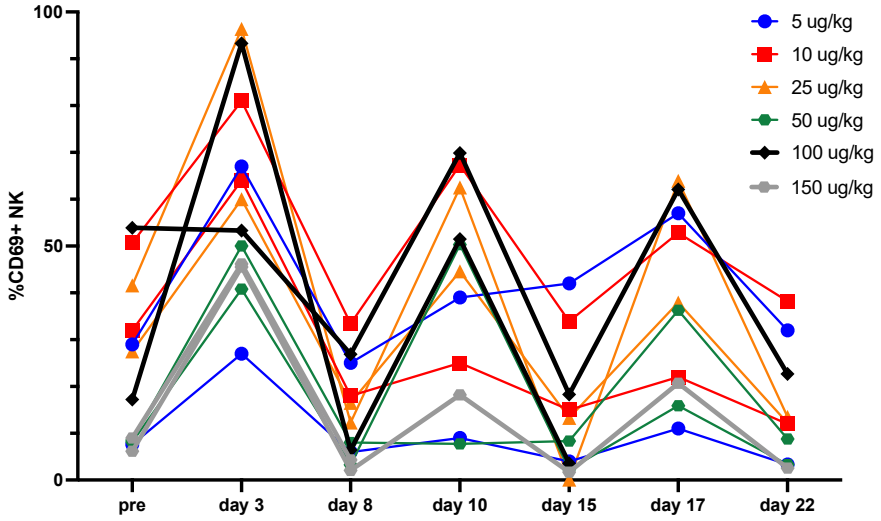




**Phase 1 (safety and dose finding)**

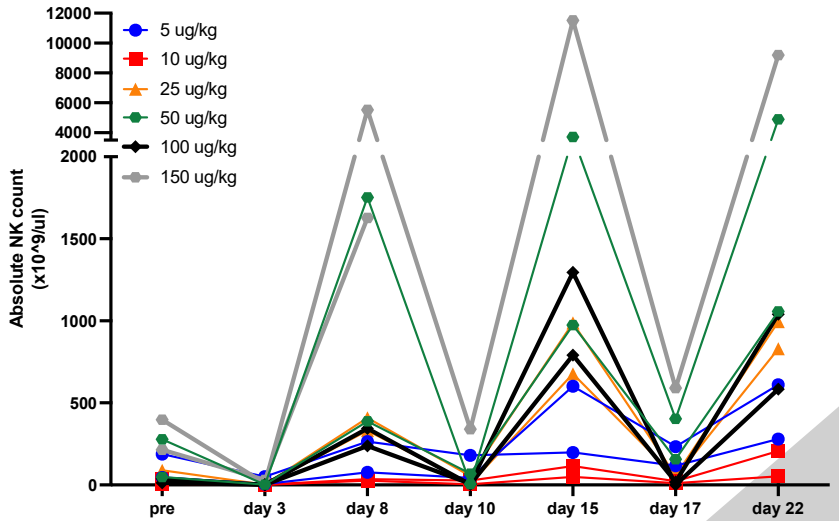
- **Six dose levels**
- **Escalation based on continual reassessment method; Cohorts of 2 subjects**
- **Day 28 (end of DLT assessment period)**

# 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%<br>Blast: 5 – 10% | Cellularity: 10 – 30%<br>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%<br>Blast: 7% | Cellularity: 90 – 95%<br>Blast: 94% | Progression |
| 3 | 10 | r/r AML. AML- 3 therapies before TriKE: 1. Azacitidine, 2. Enasidenib, 3. Hydrea | Cellularity: 100%<br>Blast: 85% | Cellularity: 100%<br>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%<br>Blast: 5.5% | Cellularity: 5%<br>Blast: 20% | Stable MDS |
| 5 | 25 | Secondary AML, progressed from MDS.<br>33% reduction in blast count | Cellularity: 10 – 15%<br>Blast: 18% | Cellularity: 20%<br>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%<br>Blast: 29% | Cellularity: 10 – 20%<br>Blast: 35% | Mild blast increase |
| 7 | 50 | HR MDS. MDS - 3 therapies: 1. Decitabine, 2. Luspatercept, 3. Decitabine 10 day<br>61.7% reduction in blast count | Cellularity: 70 – 80%<br>Blast: 12% | Cellularity: 60%<br>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%<br>Blast: 12% | Cellularity: 30%<br>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<br>63.6% reduction in blast count | Cellularity: 20%<br>Blast: 22% | Cellularity: 10 – 20%<br>Blast: 8% | Partial remission |
| 10 | 100 | r/r AML. Breast Cancer: 4 therapies: 1. Masectomy/LN dissection, 2. XRT, 3. Adriamycin/Cyclophosphamide, 4. Taxol. | Cellularity: 10%<br>Blast: 17% | Cellularity: 40%<br>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<br>50% reduction in CD33+ blast count | Cellularity: 25%<br>Blast: 80% | Cellularity: 80%<br>Blast: 73% | Blast reduction by FLOW |
| 12 | 150 | r/r AML - 2 therapies: 1. FLAG-IDA + venetoclax, 2. Decitabine | Cellularity: 30 – 40%<br>Blast: 36% | Cellularity: 60 %<br>Blast: 64% | Disease Progression |

# Selected Financial Information

| ASSETS | UNAUDITED AS OF MAR 31, 2025 | AUDITED AS OF DEC 31, 2024 |
|---|---|---|
| Cash + Short Term Investments | $ 2,458,000 | $ 4,044,000 |
| Other Assets | 293,000 | 188,000 |
| Total Assets | 2,658,000 | 4,232,000 |
| **LIABILITIES** | | |
| Accounts Payable + Accrued Expenses | $ 3,512,000 | $ 5,650,000 |
| Other Liabilities | - | - |
| Warrant Liability | 126,000 | 252,000 |
| Total Liabilities | 3,638,000 | 5,902,000 |
| **STOCKHOLDERS' EQUITY (DEFICIT)** | | |
| Total Stockholders' Equity (Deficit) | $ (980,000) | $ (1,670,000) |