



GT BIOPHARMA

Tri-specific NK cell engagers (TriKE[®])

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

September 2023

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Investment Opportunity – Next Generation of NK Cell Engagers

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 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

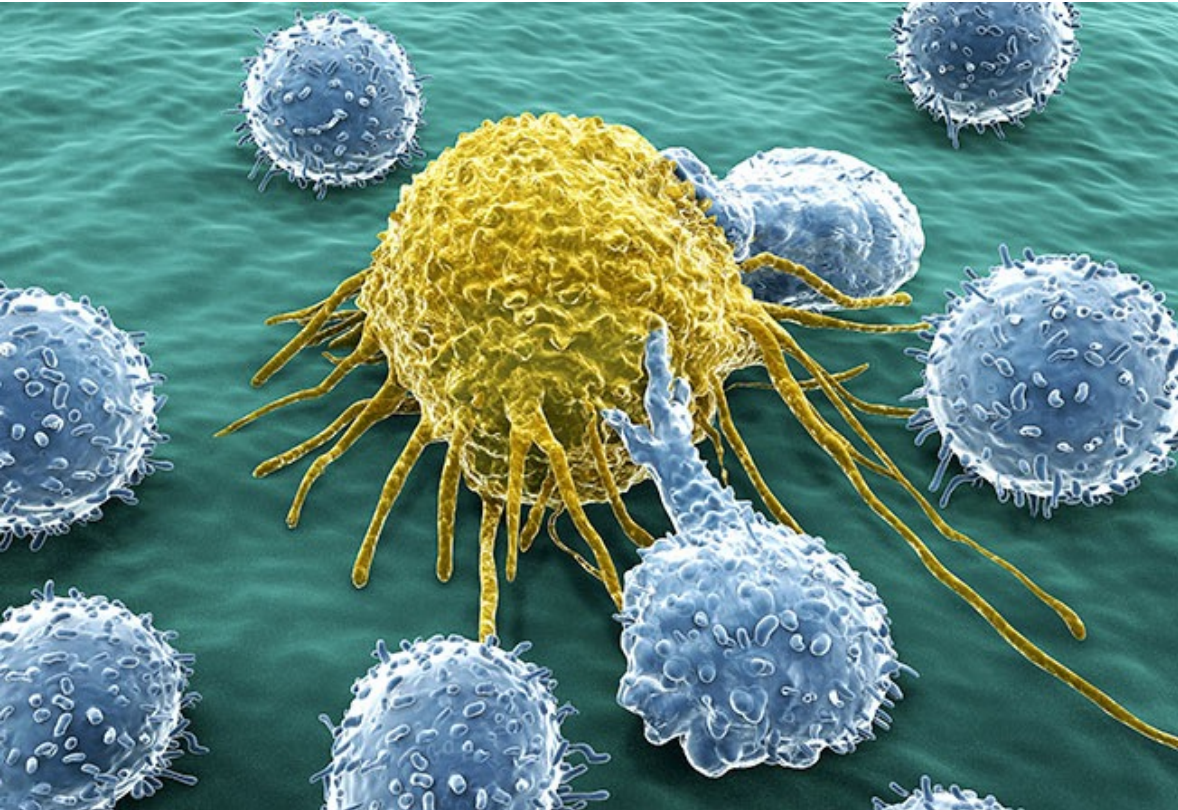
Multiple Catalysts

- 6+ pipeline assets in active preclinical development targeting both solid tumors and hematological malignancies
- Multiple INDs expected in 2023

Well-funded Experienced Leadership

- Management team with deep expertise in all stages of oncology drug development
- \$20.8 MM + in cash provides runway into 2024

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

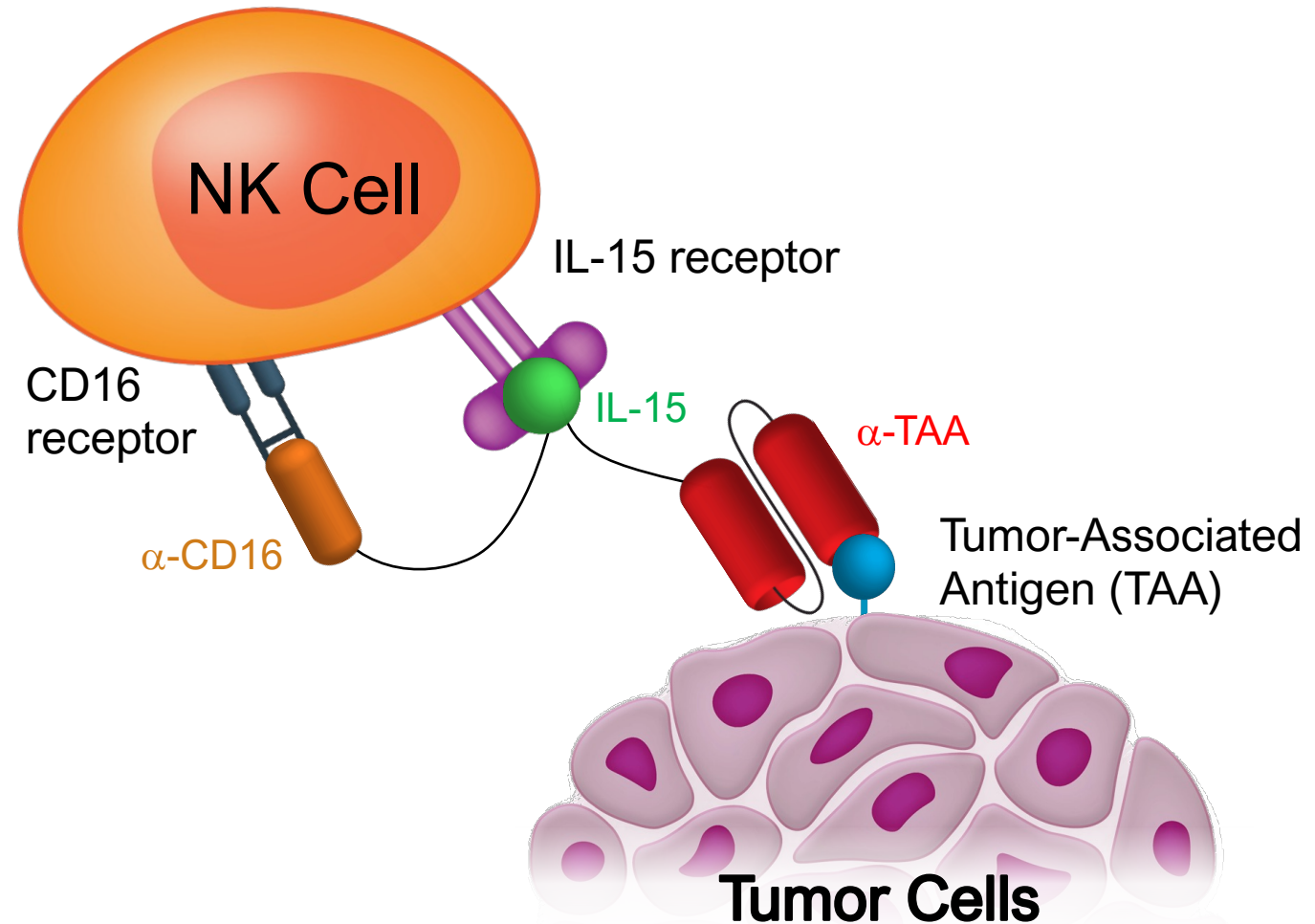
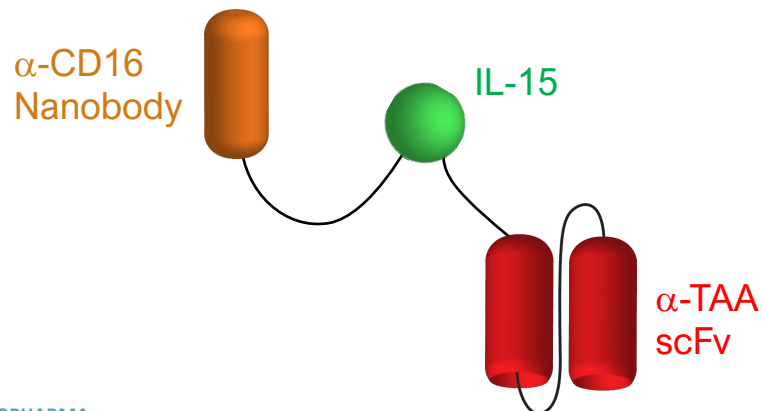
- TriKE[®] nanobody platform designed to activate endogenous NK cells to target specific cancer cells
- Potential for less toxicity than other cellular therapies such as CAR-T therapy
 - Less cytokine release syndrome (CRS)
 - Fewer neurological complications

TriKE[®]: Tri-Specific Natural Killer (NK) Cell Engagers - A Modular Platform

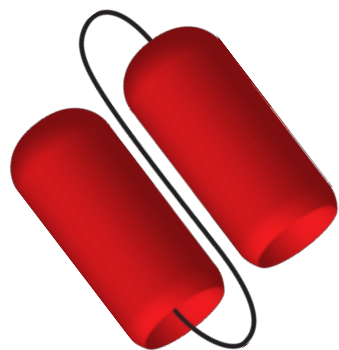
Proprietary platform utilizing camelid nanobody technology designed to bridge NK cells to tumor cells while inducing NK cell activation and expansion at the site of the tumor to enhance killing

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



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



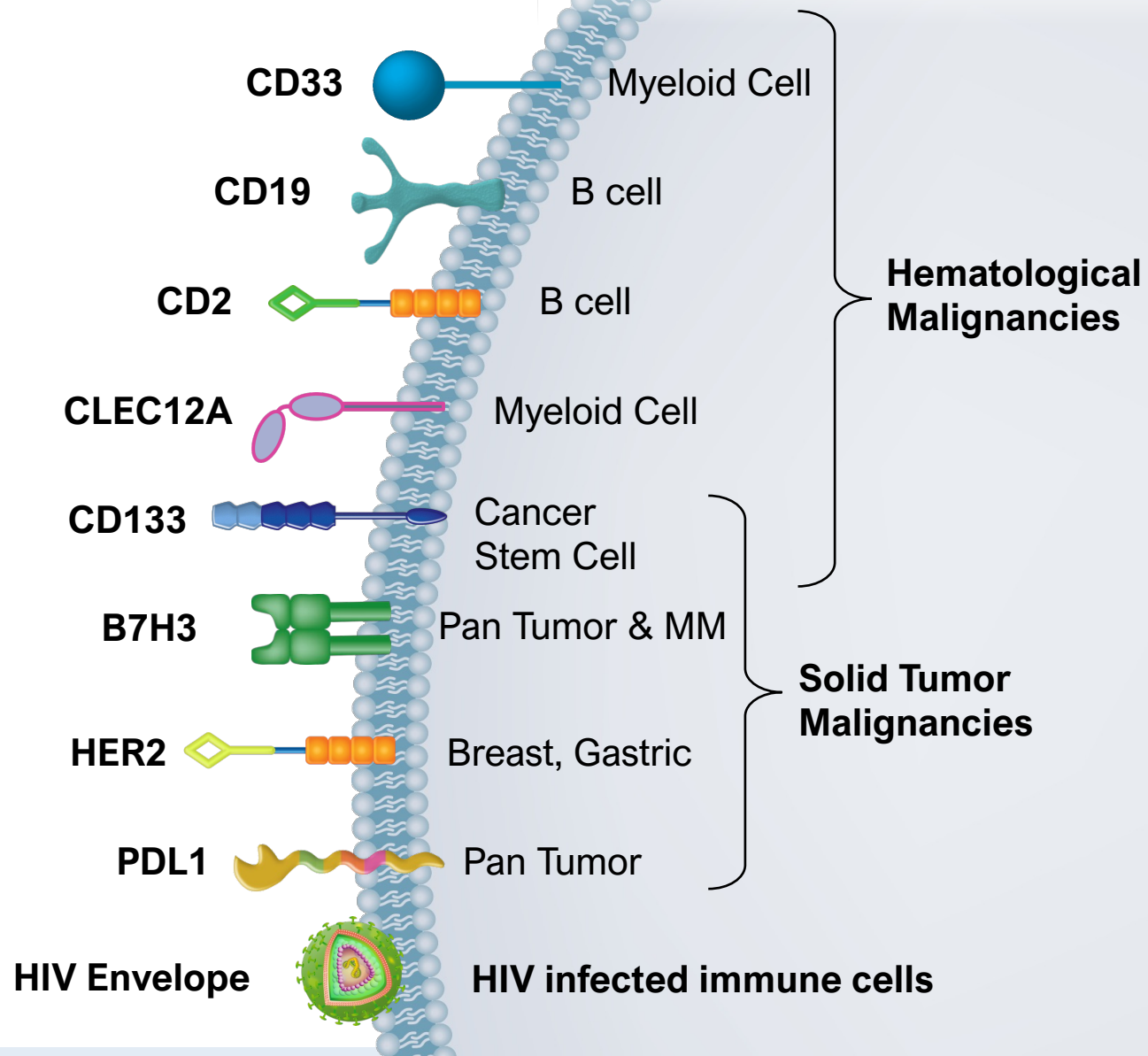
scFv



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



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-7550	Monotherapy & Combination	CD19	B-Cell Malignancies				
GTB-1050	Monotherapy & Combination		HIV				
Undisclosed Candidates	Monotherapy & Combination		Solid & Hematological Malignancies				

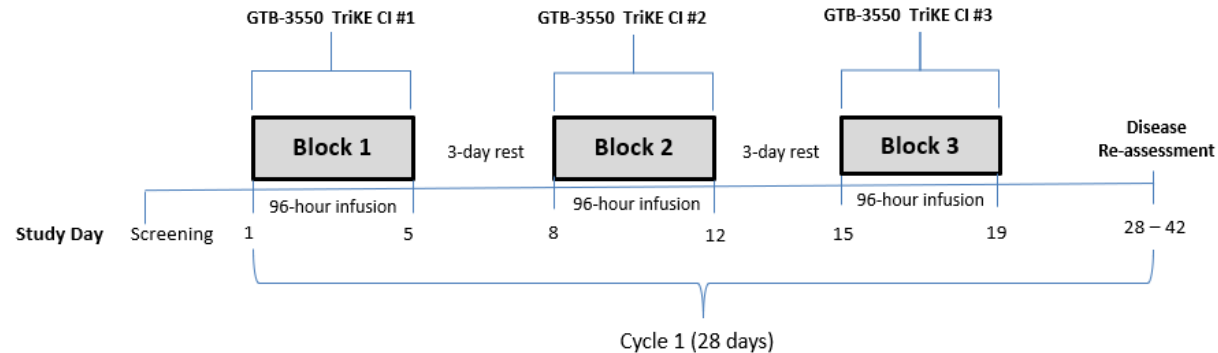
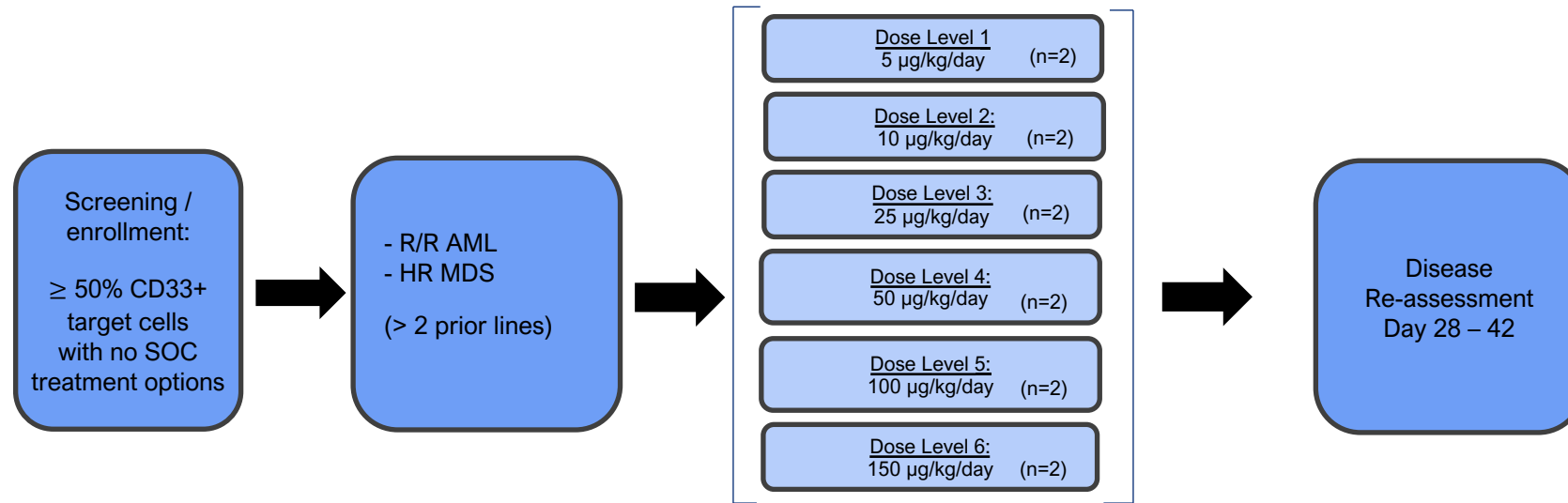
* GTB-3550 supplanted by second generation nanobody GTB-3650



GTB-3550 for AML and MDS

First generation TriKE® provides POC for platform

GTB-3550 AML/MDS Phase 1 Study Design

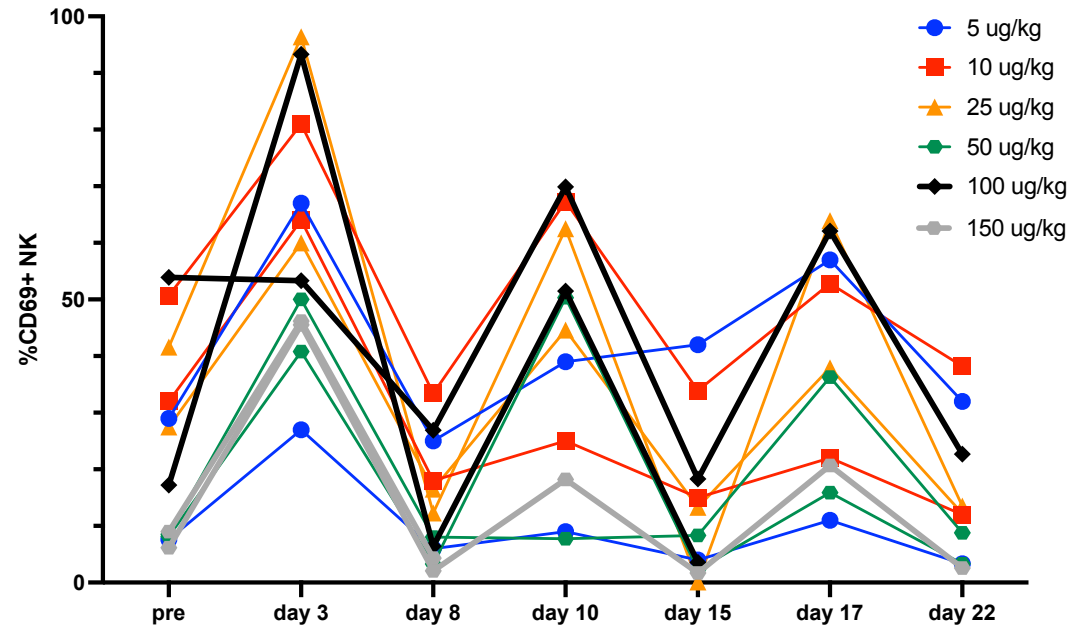


Phase 1 (safety and dose finding)

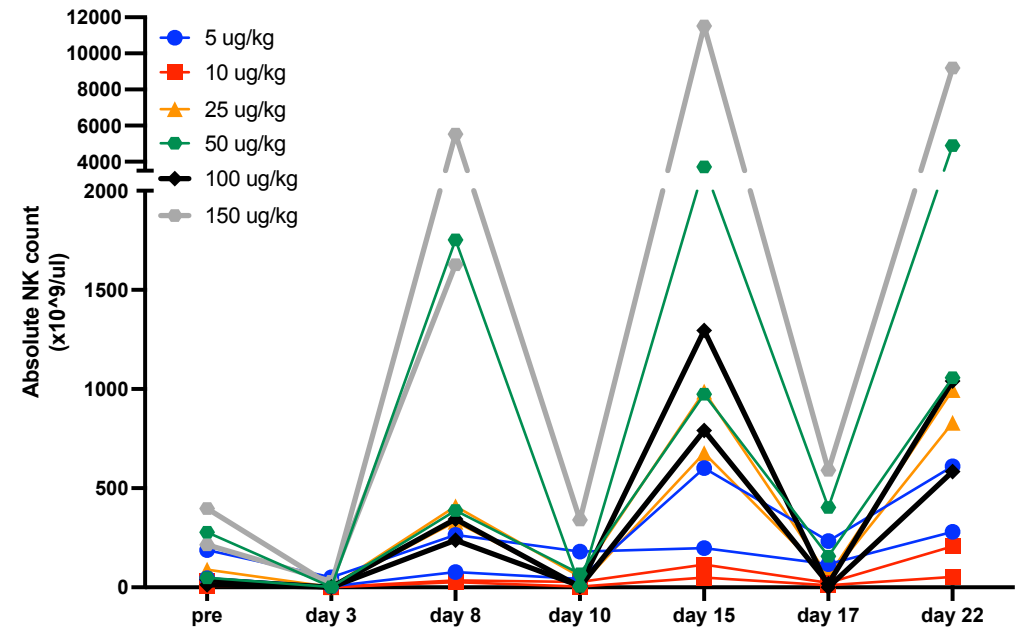
- Six dose levels
- Escalation based on continual reassessment method; Cohorts of 2 subjects
- Day 28 (end of DLT assessment period)

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)



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 TriKE: 1. 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 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 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 (T_{1/2}) of 2.2 and 2.52 hours, respectively

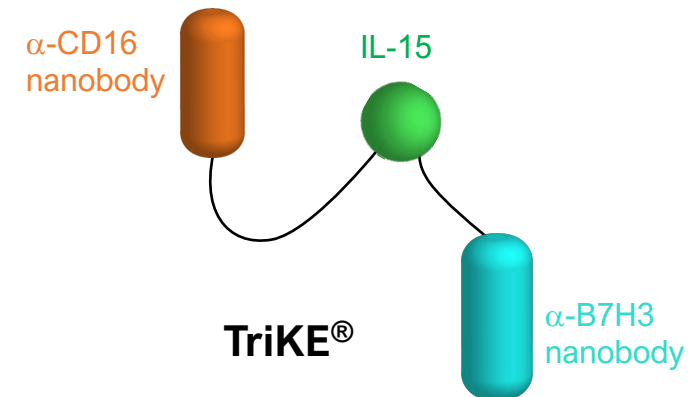
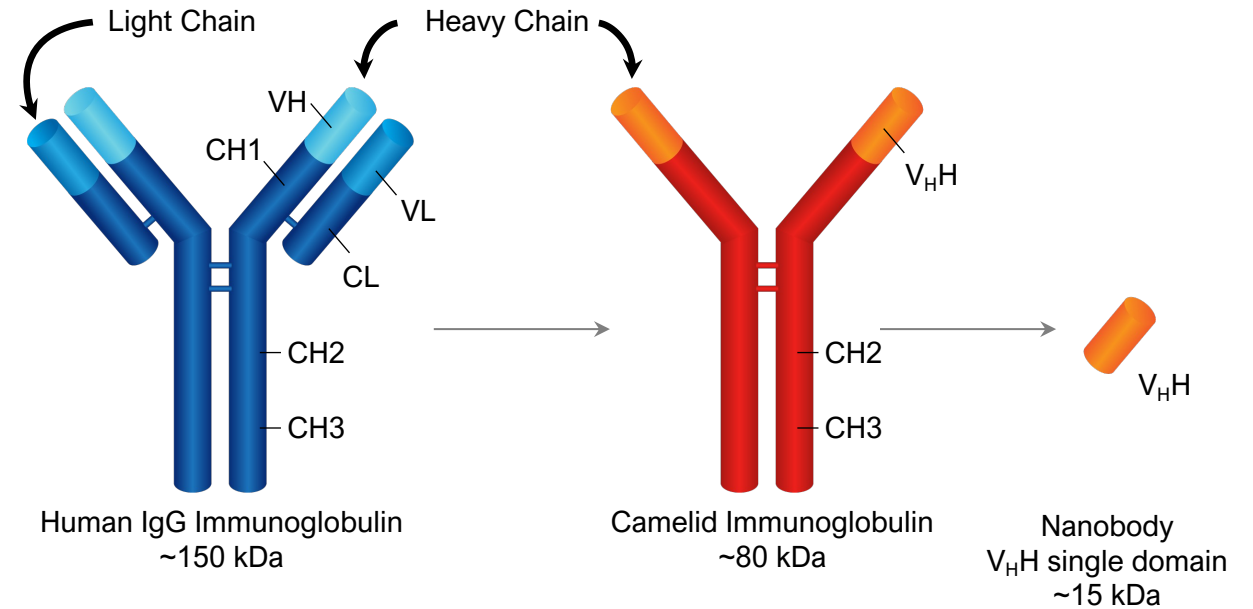


2nd Generation TriKE's

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 (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



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

TriKE® Competitive Differentiation

- The anti-CD16 component of the TriKE binds FcR γ III with high affinity compared to ADCC mediated strategies that bind with 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.





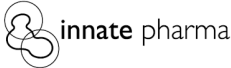







- NK cell engager/antibody therapeutic strategies designed to engage CD16, NKG2D, or NKp30
- None of them co-stimulate CD16 and IL-15 simultaneously



- NK cell therapy
- Significantly more expensive
- Could be used in combination with TriKEs

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

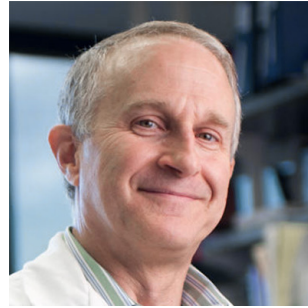
Proven record in biotech, pharma, product development, financing



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



Manu Ohri, CPA, MBA
Chief Financial Officer



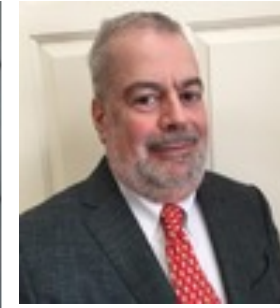
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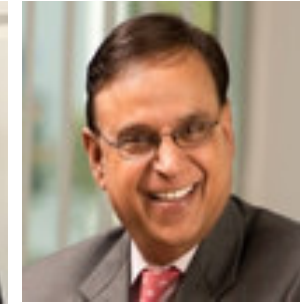
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