



***Clinical Stage Company***  
***NASDAQ: GTBP***

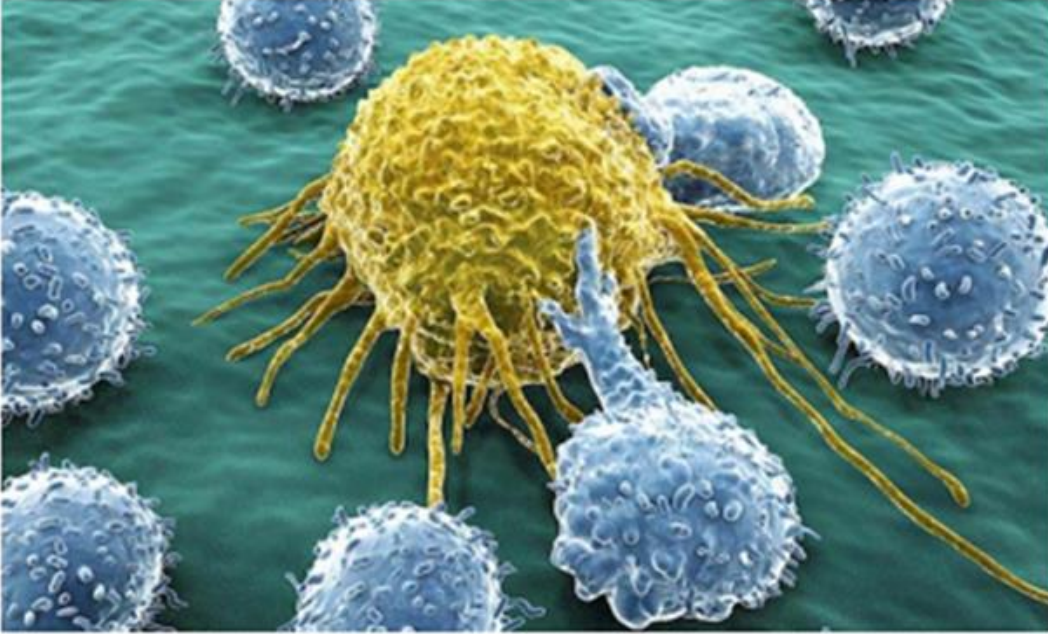
July 2021

# 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, 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.

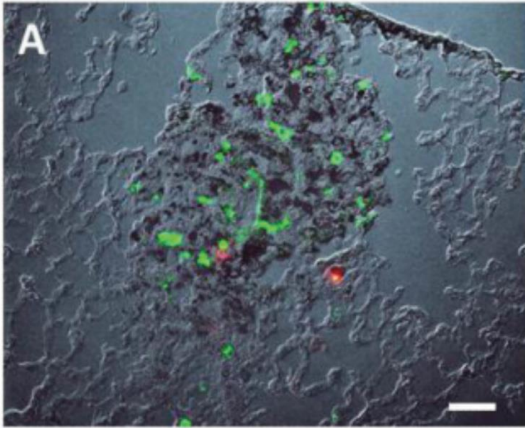
This presentation is made pursuant to Rule 163B under the Securities Act of 1933, as amended, and is intended solely for investors that are either qualified institutional buyers or institutions that are accredited investors (as such terms are defined under Securities and Exchange Commission rules) solely 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>.

# ***COMPANY FOCUS – HARNESSING NATURAL KILLER CELLS TO FIGHT CANCER***

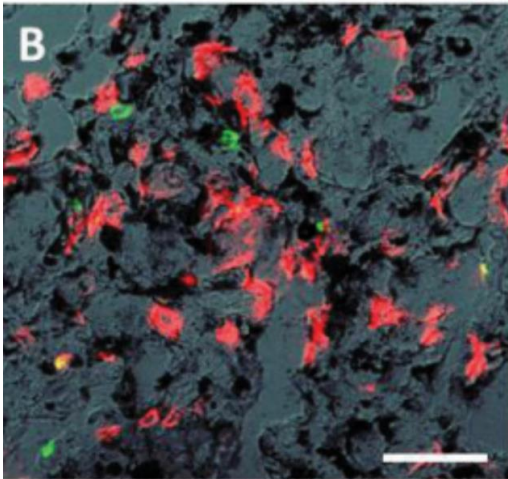


- Natural Killer (NK) cells are cytotoxic lymphocytes of the innate immune system.
- NK cells are analogous to cytotoxic T-cells of the adaptive immune system.
- NK cells are early responders that recognizes and kills stressed cells in the absence of antibodies and MHC antigen presentation, allowing for a much faster immune response.
- NK cells destroy cancer cells missing MHC markers.
- TriKE™ is an immune oncology protein therapeutic which activates NK cells, and directs them to specific cancer cell targets. TriKE™ is not a cell therapy.

# THERAPEUTIC STRATEGY



A: No NK cell proliferation within the TME.

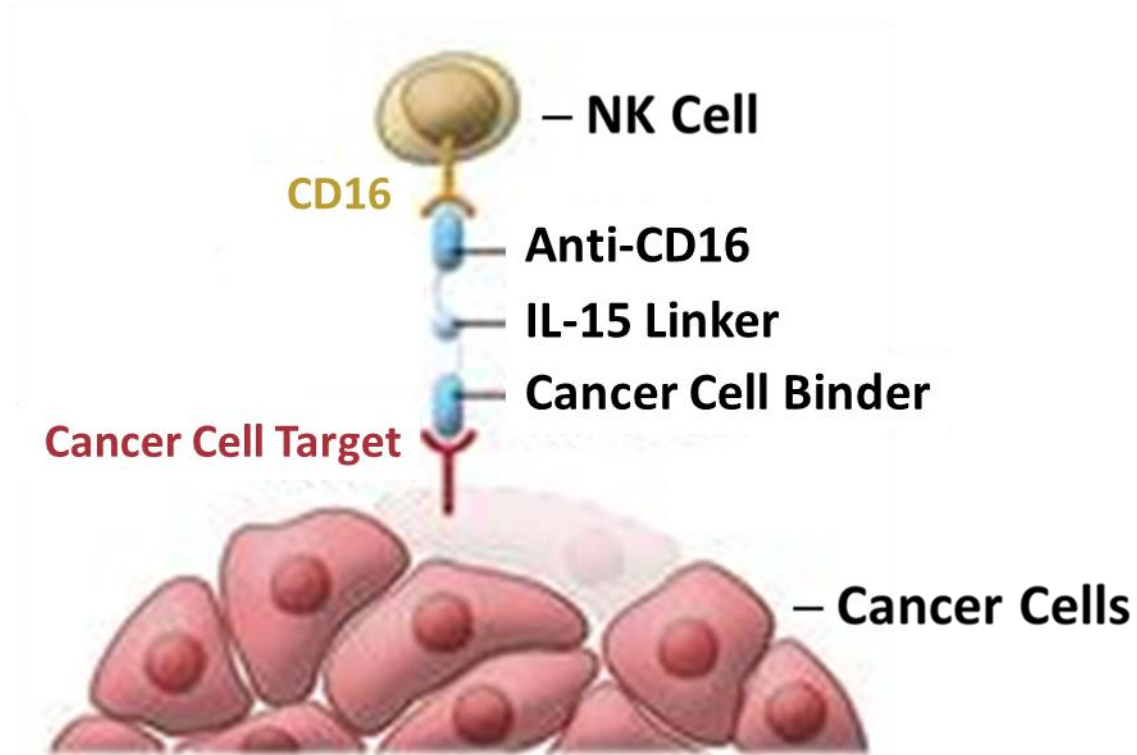


B: NK cell (red) proliferation within the TME.

Larsen, S., *Crit Rev Oncog.* (2014) 19(0): 91–105

- Restore patient's exhausted/inhibited endogenous NK cell population to again recognize and kill cancer cells.
- Integrate targeted CD16 activation and IL-15 cytokine support in a single therapeutic to drive:
  - Endogenous NK cell activation and persistence for enhanced, target-directed serial killing of cancer cells.
  - Increase endogenous NK cell proliferation
- No need for administration of supplemental *ex vivo* engineered NK cells.
- Minimize toxicities such as cytokine release syndrome (CRS) resulting from hyperactivation of T-cells.
- Treat hematologic cancers and solid tumor cancers.
- Create an immune oncology protein therapeutic – not a cell therapy.

# WHAT IS A TRIKE™ THERAPEUTIC?



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

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

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







# ***TRIKE™ DIRECTED NK CELL SERIAL KILLING OF AML CANCER CELLS***



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

- Integrated CD16 and IL-15 in TriKE drives:
  - NK cell ADCC activation for enhanced serial killing of cancer cells.
  - NK cell proliferation.
  - NK cell persistence.
- TriKE minimizes toxicities such as cytokine release syndrome (CRS) resulting from hyperactivation of T-cells.
- TriKE therapeutics can be used to treat solid tumors and hematological cancers.
- TriKE is an immune oncology protein therapeutic – not a cell therapy.

# TRIKE™ PRODUCT CANDIDATE PIPELINE

TriKE™ Product Candidates (Indication)	Pre-clin	GMP Manufacturing	Phase I	Phase II	Anticipated Time to Next Milestone
GTB-3550 TriKE (Leukemia – AML, MDS and other CD33+ Cancers)					2Q21 End of Phase I
GTB-4550 (PD-L1 / Solid Tumor Cancers)					4Q21
GTB-5550 (B7H3 / Solid Tumor Cancer)					4Q21
GTB-6550 (HER2 / Breast & Gastric Cancer)					4Q21

# GTB-3550 TRIKE™ PRODUCT CANDIDATE

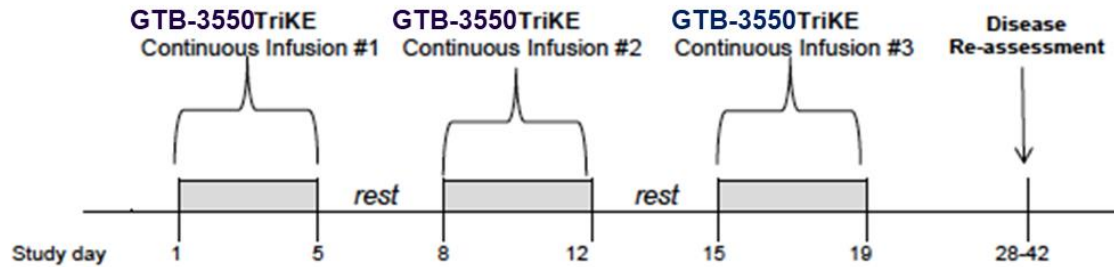


- First-in-Class immune oncology therapy.
- Target-directed NK cell ADCC killing of CD33+ hematological cancers.
- Incorporates IL-15 within therapeutic for enhanced NK cell proliferation and persistence.
- Currently being evaluated in a First-in-Human Phase I/II Expansion clinical trial.



# GTB-3550 TRIKE™ FIRST-IN-HUMAN CLINICAL TRIAL DESIGN

Phase 1 Schedule



## Phase 1: Safety and RP2D Determination

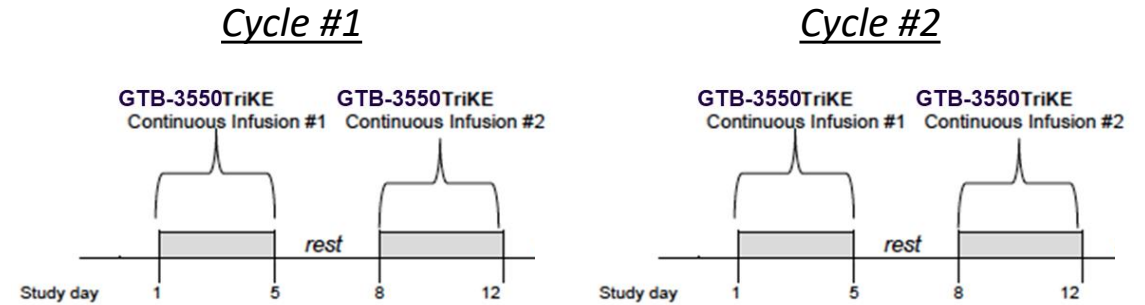
Patients will receive GTB-3550 at the assigned dose level. Patients will receive GTB-3550 at the assigned dose for three consecutive weekly 96 hour continuous infusions separated by a 72 hour rest.

### GTB-3550 Dose daily continuous infusion dose (µg/kg/day)

5  
10  
25  
50  
100  
150  
200

Objectives: To evaluate safety, identify the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) of GTB-3550 defined as the dose level that most closely corresponds to a dose limiting toxicity rate (DLT) of 20%.

Phase 2 Schedule



2-3 Week Rest Between Cycle #1 and Cycle #2

## Phase 2: Refocused on Efficacy & Durability at RP2D

- Enroll patients having CD33 blast expression level  $\geq 50\%$ .
- Three independent cohorts (higher-risk myelodysplastic syndrome, acute myeloid leukemia, and minimal residual disease).
- Treat patients with two cycles of GTB-3550 therapy with a rest period between cycles #1 and #2 as opposed to the single-cycle used during Phase 1.
- Enroll patients with fewer prior treatment lines.
- Evaluate the potential use of minimal residual disease (MRD) based endpoints that may allow for accelerated approval.

Objectives: Efficacy, durability of the clinical response, and overall survival with the goal to seek accelerated approval.

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

Patient	Dose Level	Disease and Prior Treatment History	Disease Characteristics Before GTB-3550 Therapy	Disease Characteristics After GTB-3550 Therapy
1	5 mcg/kg/day	Therapy-related AML. Failed 3 lines of induction therapy.	Cellularity: 10% Blasts: 5-10%	Cellularity: 10-20% Blasts: 10%
2	5 mcg/kg/day	AML w/ FLT-3 ITD mutation. Induction therapy x2, with CRi. Relapse, then 2x therapy with refractory disease.	Cellularity: 70-80% Blasts: 5-7%	Cellularity: 90-95% Blasts: 94%
3	10 mcg/kg/day	AML. Azacitidine x1 year with disease control before progression. Brief remission with Venetoclax + cytarabine. No response to IDH2 inhibitor.	Cellularity: 100% Blasts: 85%	Cellularity: 100% Blasts: 92%
4	10 mcg/kg/day	Therapy-related MDS. Residual disease after HMA and HMA+ Venetoclax.	Cellularity: < 5% Blasts: 10-20%	Cellularity: < 5% Blasts: 10-20%
5	25 mcg/kg/day	Secondary AML. 18 month CR with Venetoclax + Azacitidine prior to relapse. Unique FLT-3 mutation not responsive to Gilterinib.	Cellularity: 10-15% <b>Blasts: 18%</b>	Cellularity: 20% <b>Blasts: 12%</b>
6	25 mcg/kg/day	AML. Failed reinduction with Ventoclax and HMA	Cellularity: 10-25% Blasts: 29%	Cellularity: 10-20% Blasts: 35%
7	50 mcg/kg/day	MDS/MPN with Red Cell transfusion dependence post HMA and Luspatercept	Cellularity: 70-80% <b>Blasts: 12%</b>	Cellularity: 60% <b>Blasts: 4.6%</b>
8	50 mcg/kg/day	High Grade MDS. 7 year remission post UCB HCT. Post-HCT relapse treated with Azacitidine Remission duration: 1 year prior to disease progression Concurrent asymptomatic smoldering myeloma	Cellularity: 20% Blasts: 12% Concurrent smoldering myeloma 20% plasma cells	Cellularity: 30% Blasts: 19% Concurrent smoldering myeloma with 20-25% plasma cells
9	100 mcg/kg/day	High Grade MDS: Azacitidine, Decitabine, 7+3, MUD RIC HCT Relapse Day +100, Progression to AML, Lack of Response to Decitabine + Venetoclax	Cellularity: 10% <b>Blasts: 22%</b>	Cellularity: 10-20% <b>Blasts: 8%</b>

## Clinical Efficacy Demonstrated:

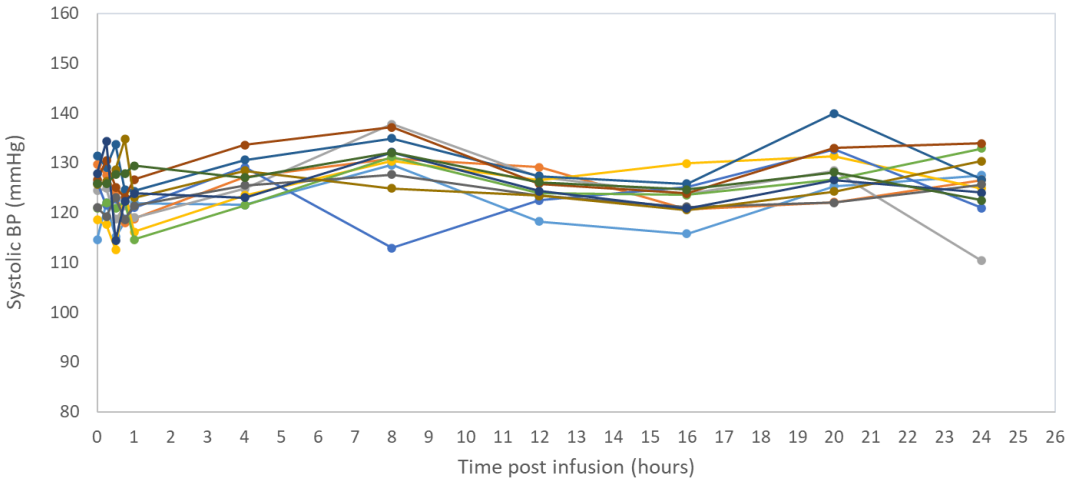
- Patient 5: 33.3% Reduction in Blast Levels
- Patient 7: 61.7% Reduction in Blast Levels
- Patient 9: 63.6% Reduction in Blast Levels

# GTB-3550 TRIKE™ Is Well Tolerated By Patients

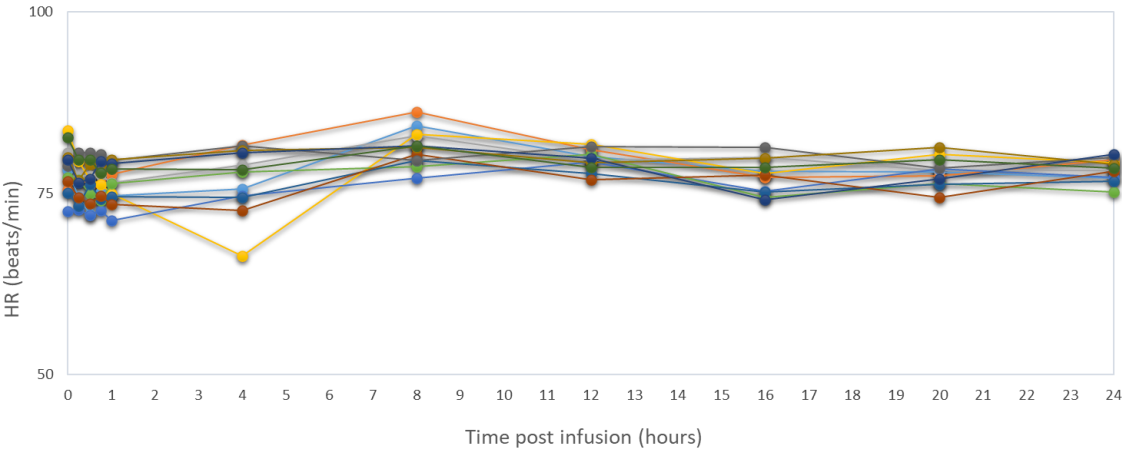
**Panel A:** Dose Equivalent of GTB-3550 and Systemic Maximum Therapeutic Dose of IL-15

PER MOLE BASIS	
Dose of GTB-3550 (mcg/kg)	Fold Higher Than MTD rhIL-15
5	0.538
10	1.075
25	2.688
50	5.376
100	10.753
200	21.505

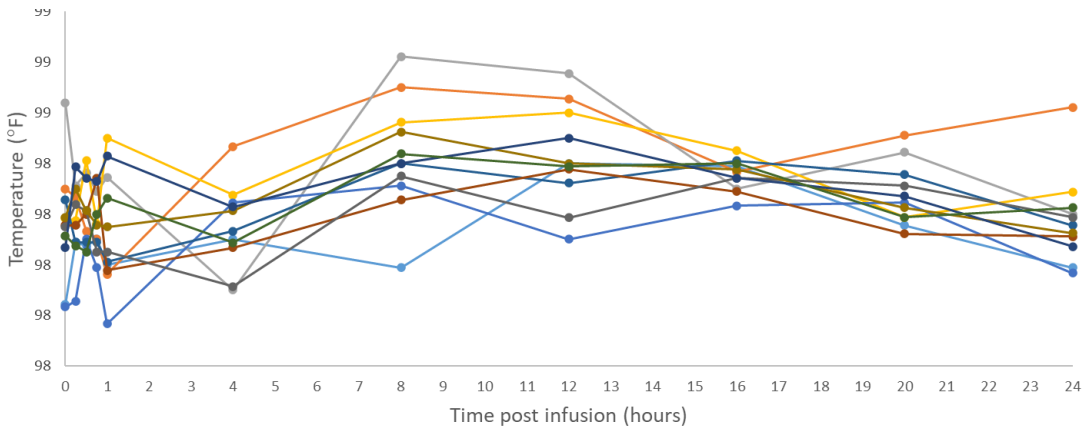
**Panel B:** Systolic Blood Pressure



**Panel C:** Heart Rate



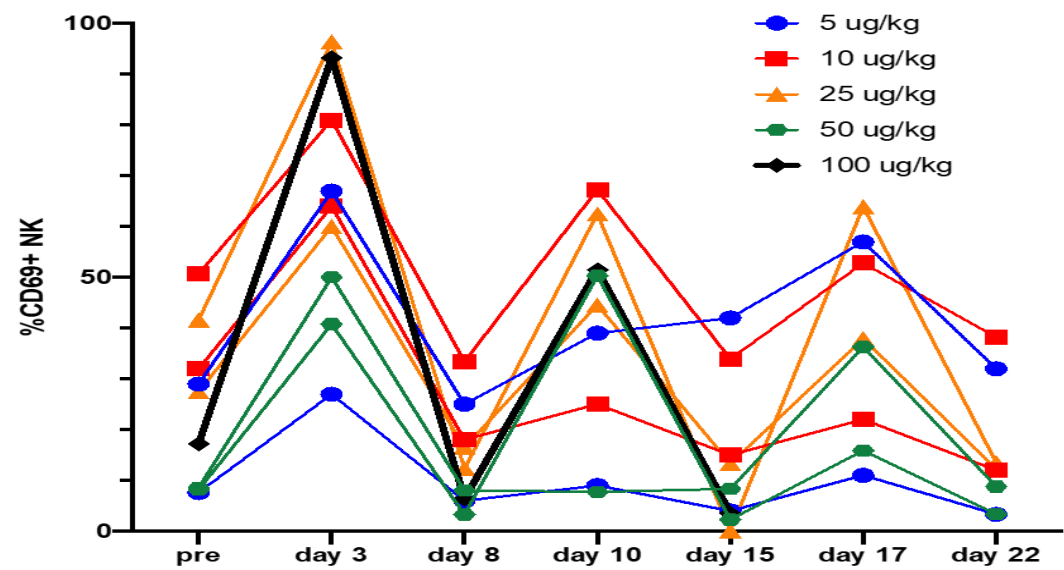
**Panel D:** Body Temperature



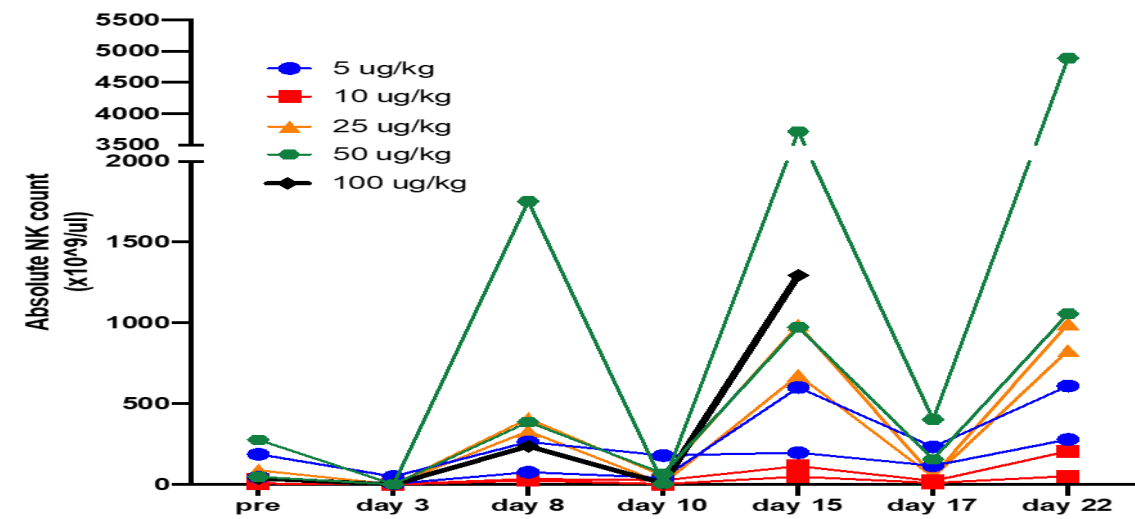
# GTB-3550 TRIKE™ FIRST-IN-HUMAN CLINICAL TRIAL INTERIM RESULTS

## TriKE™ activates Patient's endogenous NK cells in the periphery and they egress into tissues

Panel A: Increase in NK cell activation upon administration of GTB-3550.

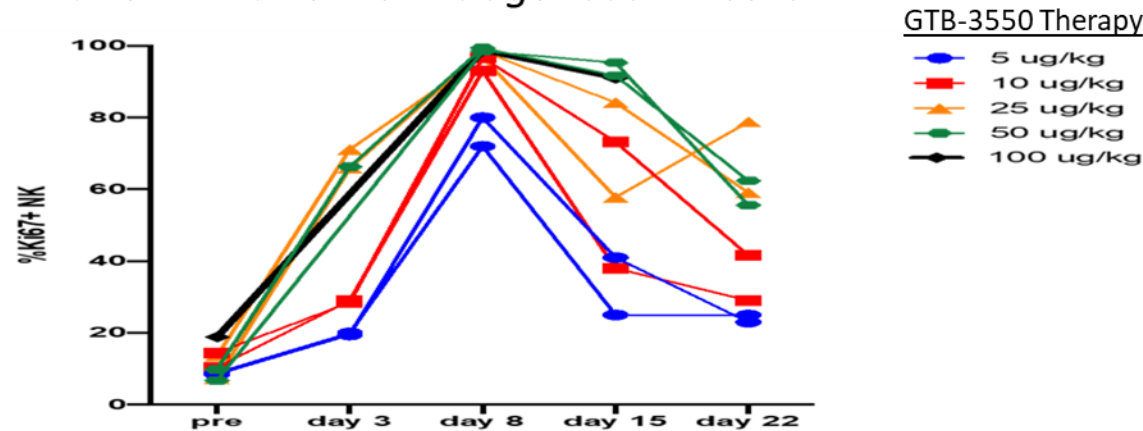


Panel B: Increase in absolute number of NK cells during treatment.



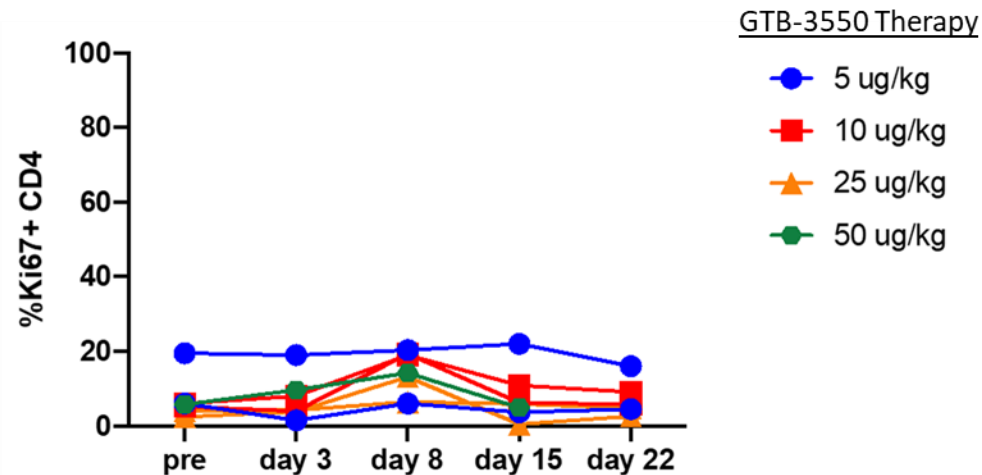
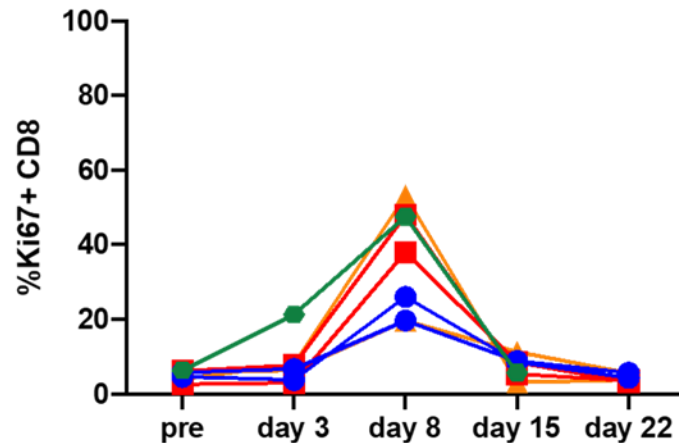
# GTB-3550 TRIKE™ FIRST-IN-HUMAN CLINICAL TRIAL INTERIM RESULTS

Panel A: Patient's Endogenous NK cells



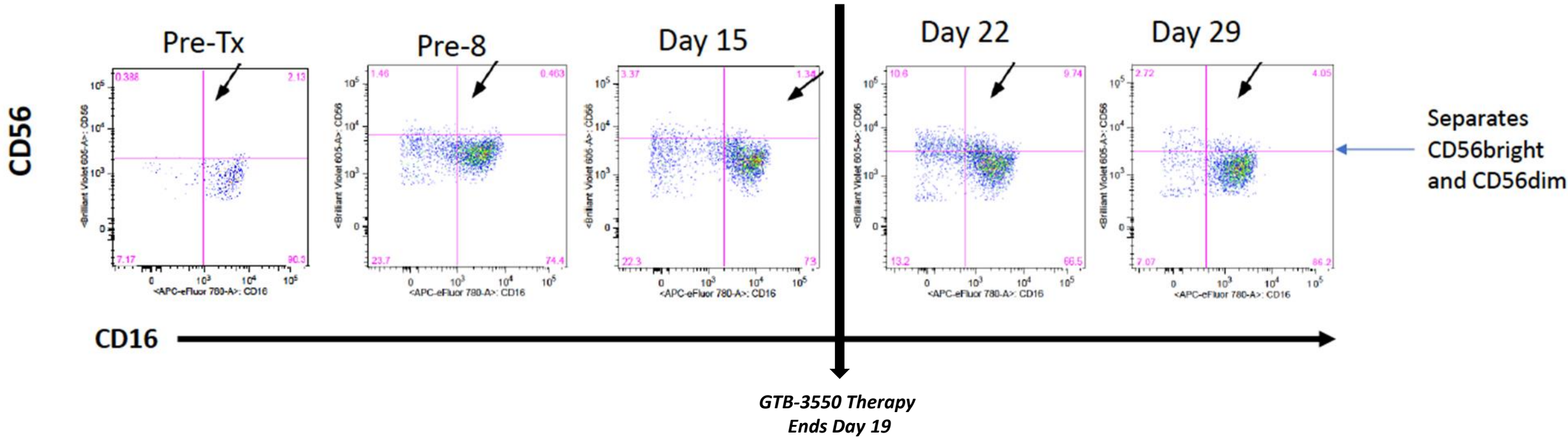
- TriKE-directed proliferation of NK cells
- No hyperproliferation or hyperactivation of T-cells
- No Cytokine Release Syndrome (CRS)

Panel B: Patient's Endogenous T-cells



# GTB-3550 TRIKE™ CLINICAL TRIAL IMMUNE MONITORING RESULTS

## No Loss of CD16 During GTB-3550 Therapy



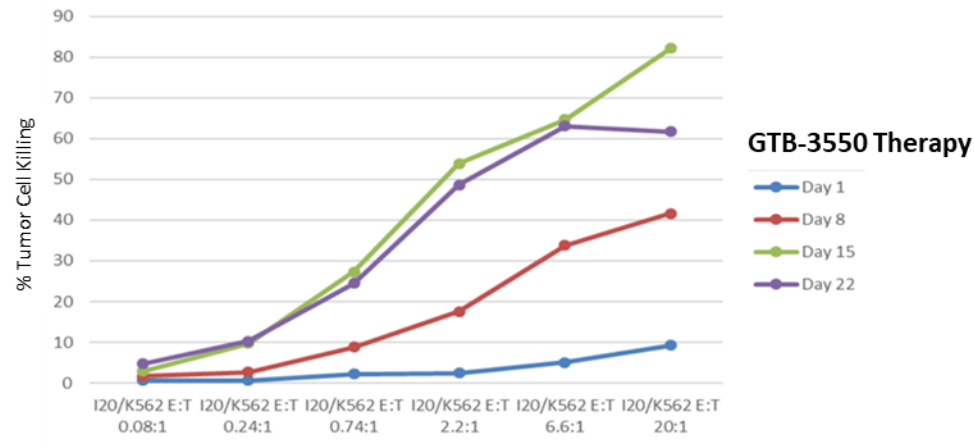
Data from patient #7 treated with 50 mcg/kg/day



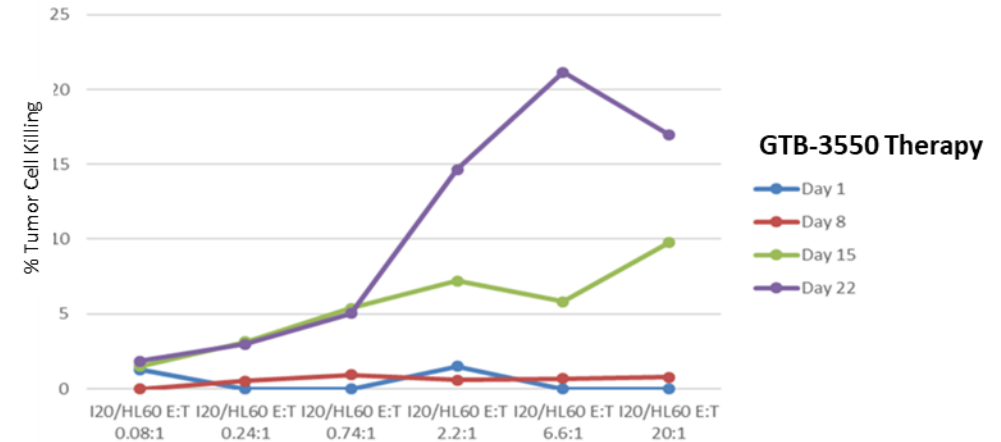
# GTB-3550 TRIKE™ FIRST-IN-HUMAN CLINICAL TRIAL INTERIM RESULTS

## TriKE Therapy Rescues Patient's NK Cells & Increases Cancer Cell Killing

K562 AML Cancer Cells + Patient's NK Cells



HL60 AML Cancer Cells + Patient's NK Cells

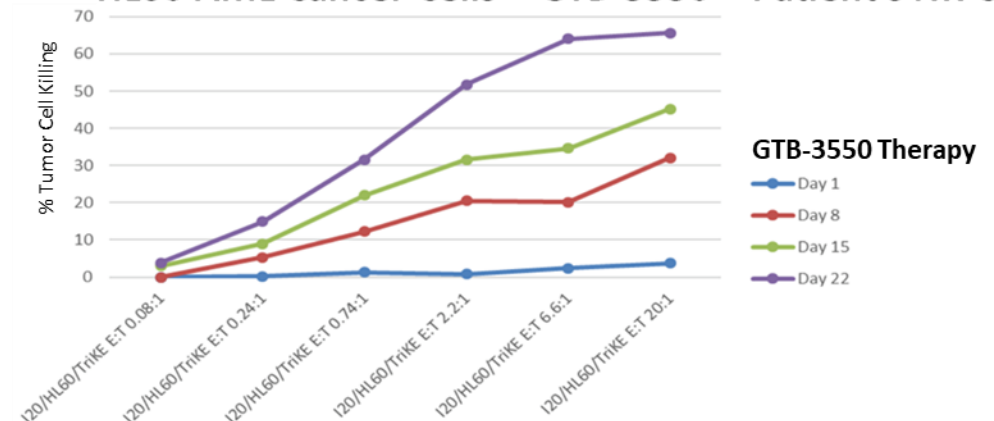


From patient #7 treated at 50 mcg/kg patient  
Lysis Measured in Standard 4 hr Chromium Release

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

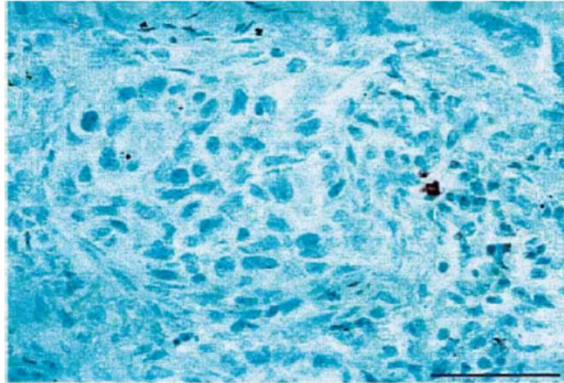


# ***GTB-3550 TriKE™ FIRST-IN-HUMAN CLINICAL TRIAL INTERIM RESULTS***

- GTB-3550 TriKE induces reproducible NK cell proliferation in all patients at all dose levels evaluated with no clinically significant toxicity. No CRS resulting from hyperactivation of patient's T-cell population.
- Clinical responses to date demonstrate strong NK cell activation, persistence, proliferation and targeted cancer cell killing.
- GTB-3550 significantly reduced bone marrow blast levels 61.7% and 63.6% in Patient 7 and Patient 9, respectively.
- 60% (3 out of 5) patients treated with doses of GTB-3550 between 25mcg/kg/day and 100mcg/kg/day demonstrated positive clinical response.
- No loss in CD16 expression on patient's NK cells. No need for supplemental NK cell therapy.

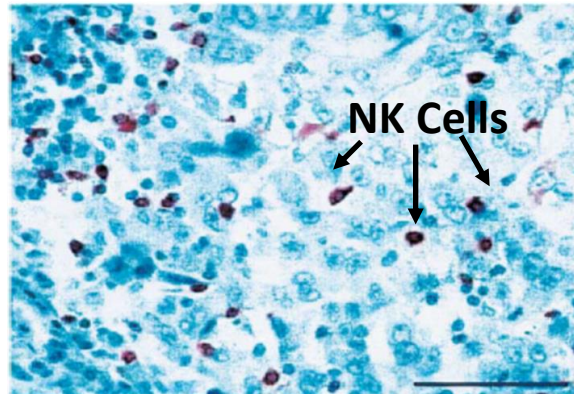
# NK CELL INFILTRATION OF TUMOR IMPROVES PATIENT SURVIVAL

Low NK Cell Infiltration



Male, 74 years of, ex-smoker. Peripheral squamous cell lung cancer, stage IB. Time survival at follow-up of 37 months (died).

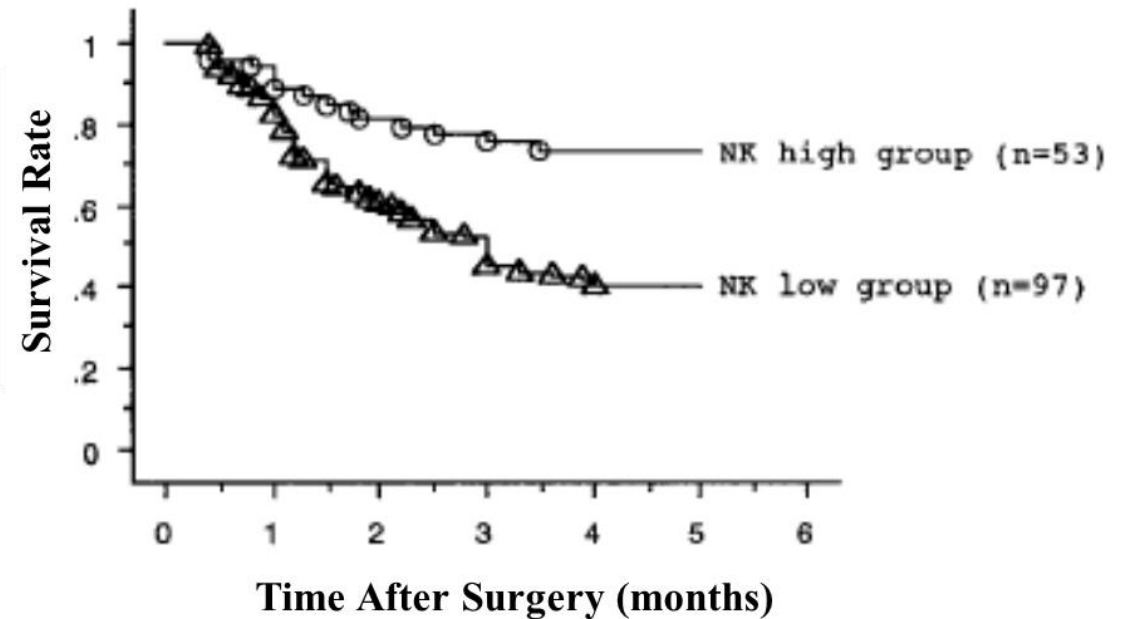
High NK Cell Infiltration



Male, 75 years old, ex-smoker. Central squamous cell lung cancer, stage IB. Time survival at follow-up of 139 months (still alive).

F.R. Villegas et al., *Lung Cancer* 35 (2002) 23–28

High vs Low NK Cell Infiltration into Tumor

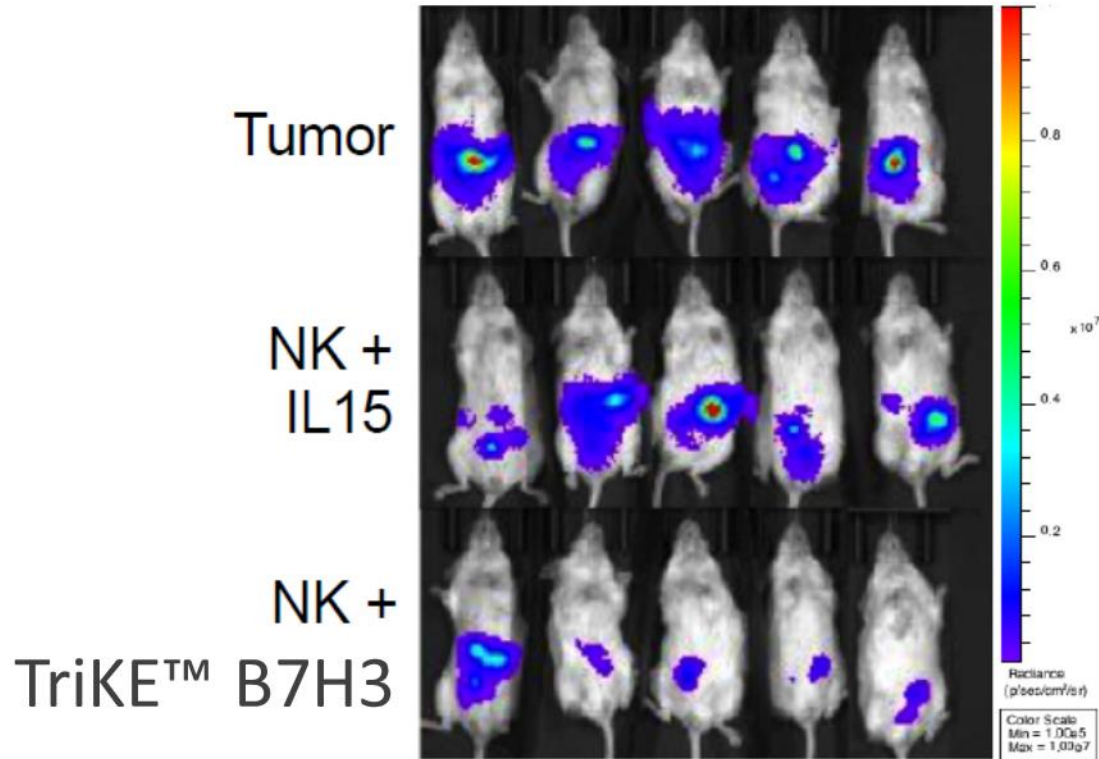


Overall survival curves of patients with pulmonary adenocarcinoma on the basis of NK cell infiltration. ( $P=0.0002$ )

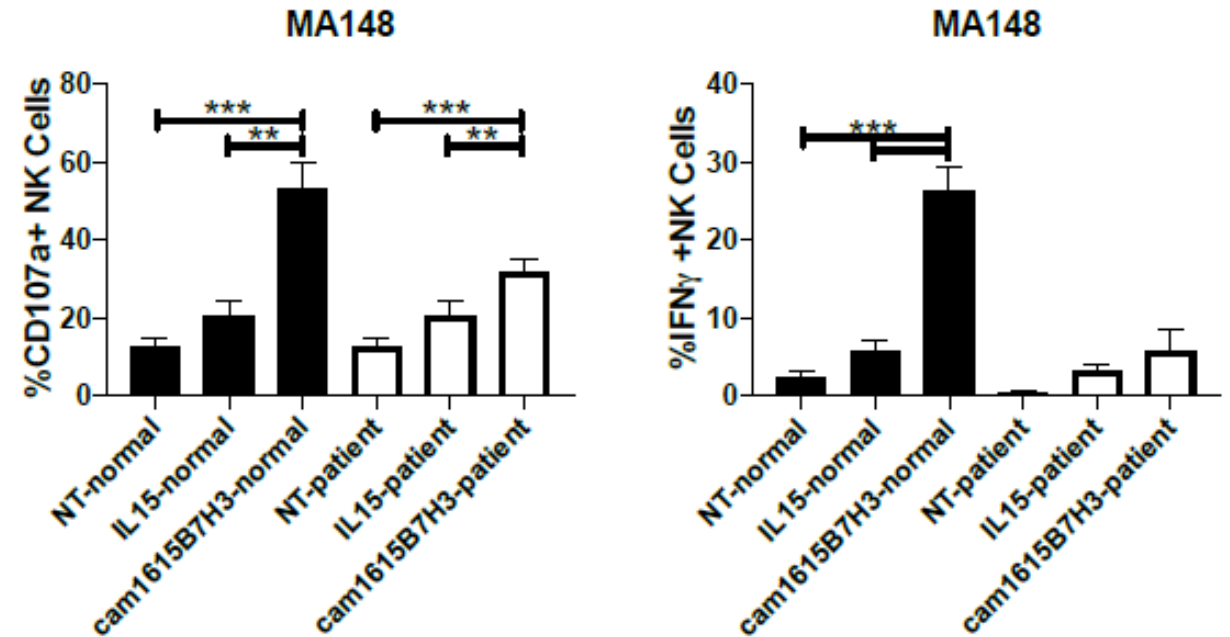
Takanami, I et al, *J Thorac Cardiovasc Surg* 2001;121:1058-63

# TRIKE™ B7H3: MULTI-CANCER STRATEGY

## Day 21 After MA-148 Tumor Implant



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

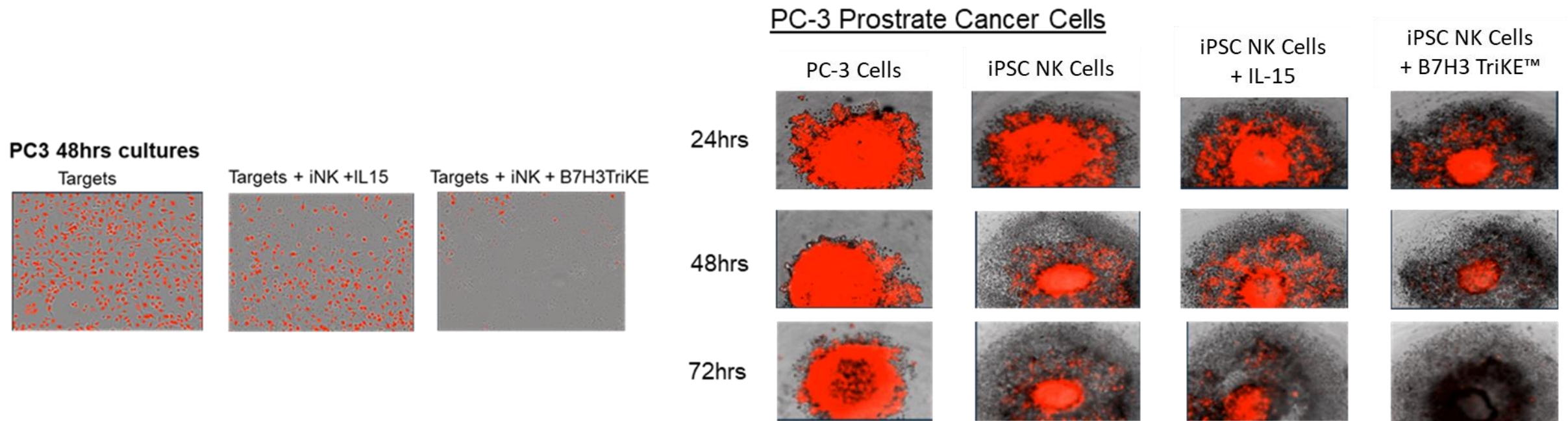


**Significant killing of MA148 Ovarian Cancer by TriKE™ B7H3**



# TRIKE™ MAKES NK CELL THERAPIES MORE EFFECTIVE

## Eradication of Prostate Cancer Cells by TriKE™ Directed iPSC NK Cells



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

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# COMPETITION

## *TriKE™ Competitive Advantages*

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



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



NK cell therapy. Significantly more expensive.



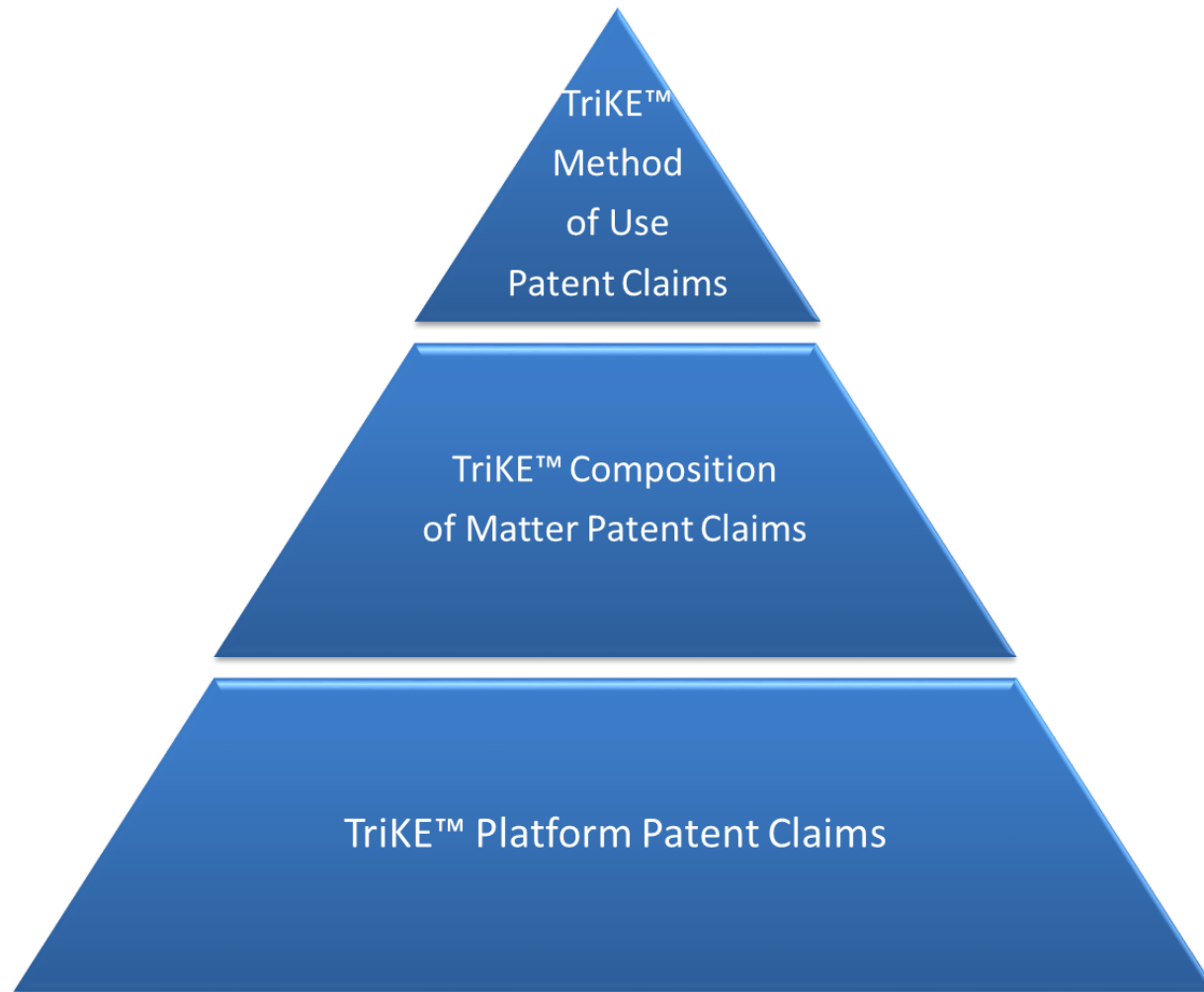
# PARTNERSHIP HIGHLIGHTS



- Cytovance will develop GMP cell lines, and manufacture TriKE product candidates for use in GT Biopharma clinical trials.
- GT Biopharma has the option to pay Cytovance in cash or shares of GT Biopharma common stock.
- Cytovance will help develop new TriKE product candidates on a fee-for-services basis – no clinical development milestone payments or royalties on product sales.
- GT Biopharma receives fully paid nonexclusive license to use Cytovance's Keystone® E. coli bacterial and CHO mammalian expression systems for the manufacture of TriKE product candidates.



# 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.



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