Clinical Stage Company
OTCQB: GTBP and Euronext/OTCMKTS: GTBP.PA

December 2020
**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, 2019, 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.
COMPANY FOCUS – HARNESING 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 recognize 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.
NK cells infiltrate tumors

NK cell infiltration of tumors improves patient outcomes and survival.

Male, 74 years old, ex-smoker. Peripheral squamous cell lung cancer, stage 1B. Time survival at follow-up of 37 months (died).

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

**THERAPEUTIC STRATEGY**

Enhance tumor cell killing by increasing the number of ADCC-activated, target-directed cytotoxic NK cells within the tumor microenvironment.

**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 ADCC Serial Killing of Tumor Cells**

- 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.
<table>
<thead>
<tr>
<th>TriKE™ Product Candidates (Indication)</th>
<th>Pre-clin</th>
<th>GMP Manufacturing</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Anticipated Time to Next Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTB-3550 TriKE (Leukema - AML and other CD33+ Cancers)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2Q21 End of Phase I</td>
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<tr>
<td>GTB-4550 (PD-L1 / Solid Tumor Cancers)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4Q20</td>
</tr>
<tr>
<td>GTB-5550 (B7H3 / Solid Tumor Cancer)</td>
<td></td>
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<td>4Q20</td>
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</table>
**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: Dose Finding (at least 12 evaluable patients)**

Patients will receive GTB-3550 at the assigned dose level. Each patient will receive a bolus test dose (20% of the daily continuous infusion dose) to assess pharmacokinetics/pharmacodynamics. If no unacceptable reactions occur after 4 hours, the patient 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)**

<table>
<thead>
<tr>
<th>Dose (µg/kg/day)</th>
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<tbody>
<tr>
<td>5</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>25</td>
</tr>
<tr>
<td>50</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>200</td>
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</tbody>
</table>

Primary Objective: To 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: Efficacy at RP2D (max 30 patients)**

Patients will receive three consecutive blocks of four 24 hour continuous infusions of GTB-3550 TriKE at the Phase I RP2D separated by a 72 hour rest.

Primary Objective: To determine preliminary efficacy as measured by the rates of “best” clinical response by Day 42 day after the start of the 1st infusion.

**Stage 1:** Enroll 13 patients, including all patients treated at the MTD during Phase 1. If 3 or more of these 13 patients have a clinical response to GTB-3550 the trial moves to Stage 2.

**Stage 2:** Enroll an additional 17 patients.
# GTB-3550 TRIKE™ First-in-Human Clinical Trial Interim Results

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Dose Level</th>
<th>Disease and Prior Treatment History</th>
<th>Disease Characteristics Pre-TRIKE</th>
<th>Disease Assessment Post TRIKE</th>
<th>Toxicity and Response Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1^</td>
<td>5 microgram/kg/day</td>
<td>Therapy-Related AML: 3 Lines Induction Chemotherapy</td>
<td>Cellularity: 10% Blasts: 5-10%</td>
<td>Cellularity: 10-20% Blasts: 10%</td>
<td>Clinically Significant Toxicity: None Disease Response: Stable AML with improved platelet transfusion needs</td>
</tr>
<tr>
<td>2</td>
<td>5 microgram/kg/day</td>
<td>FLT-3 ITD AML: Induction X 2 (\rightarrow) CR1 Relapse (\rightarrow) 2 lines therapy with refractory disease</td>
<td>Cellularity: 70-80% Blasts: 5-7%</td>
<td>Cellularity: 90-95% Blasts: 94%</td>
<td>Significant Toxicity: None Disease Response: Progressive AML</td>
</tr>
<tr>
<td>3</td>
<td>10 micrograms/kg/day</td>
<td>AML: Azacitidine X 1 year with disease control before progression Brief Remission with venetoclax + cytarabine No response to IDH2 inhibitor</td>
<td>Cellularity: 100% Blasts: 85%</td>
<td>Cellularity: 100% Blasts: 92%</td>
<td>Significant Toxicity: None Disease Response: Stable AML</td>
</tr>
<tr>
<td>4</td>
<td>10 micrograms/kg/day</td>
<td>Therapy-related MDS: Residual disease after HMA and then HMA + Venetoclax</td>
<td>Cellularity: &lt; 5% Blasts: 10-20% on CD34 stain</td>
<td>Cellularity: &lt; 5% Blasts 10-20% on CD34 stains</td>
<td>Significant Toxicity: None Disease Response: Stable AML</td>
</tr>
</tbody>
</table>
## GTB-3550 TriKE™ First-in-Human Clinical Trial Interim Results

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<tr>
<th>Patient Number</th>
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</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>25 micrograms/kg/day</td>
<td>Secondary AML: 18 month CR with Venetoclax + Azacitidine Relapse with unique FLT-3 mutation No response to Gilteritinib</td>
<td>Cellularity: 10-15% Blasts: 18%</td>
<td>Cellularity: 20% Blasts: 12%</td>
<td>Significant Toxicity: Neutropenic Fever Disease Response: Blast Reduction Improved Platelet Transfusion needs</td>
</tr>
<tr>
<td>6</td>
<td>25 micrograms/kg/day</td>
<td>Relapsed AML Failed re-induction with Venetoclax + HMA</td>
<td>Cellularity: 10-25% Blasts: 29%</td>
<td>Cellularity: 10-20% Blasts: 35%</td>
<td>Significant Toxicity: None Disease Response: Stable AML</td>
</tr>
<tr>
<td>7</td>
<td>50 micrograms/kg/day</td>
<td>MDS/MPN with Red Cell transfusion dependence post HMA and Luspatercept</td>
<td>Cellularity: 70-80% Blasts: 12%</td>
<td></td>
<td>Significant Toxicity: None</td>
</tr>
</tbody>
</table>

Blasts: 4.6%
**Panel A:** Increase in NK cell activation upon administration of GTB-3550.

**Panel B:** Significant NK cell proliferation by Day 8 with continued proliferation well above baseline during treatment.

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

**Panel D:** Patient NK cell killing demonstrating no NK cell exhaustion after continuous GTB-3550 therapy.
No Hyperactivation of T-cells
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**

**Increased Target Cell Killing**

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
Interim Results to Date

• 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 GTB-3550 TriKE immune activity and targeted cancer cell killing in humans.

• At the 50mcg/kg/day dose level, GTB-3550 therapy reduced blast levels in bone marrow from 12% before therapy to less than 5% post therapy. Clinical benefit achieved – patient became eligible for HSCT.

• No loss in CD16 expression on patient’s NK cells. No need for supplemental NK cell therapy.
Enhance tumor cell killing by increasing the number of ADCC activated, target-directed cytotoxic NK cells within the tumor microenvironment.

<table>
<thead>
<tr>
<th>Cancer type</th>
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<tbody>
<tr>
<td>Colorectal carcinoma</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Gastric carcinoma</td>
</tr>
<tr>
<td>Adenocarcinoma lung</td>
</tr>
<tr>
<td>Gastric carcinoma</td>
</tr>
<tr>
<td>Leukemia</td>
</tr>
<tr>
<td>Squamous cell, lung</td>
</tr>
<tr>
<td>Renal cancer</td>
</tr>
<tr>
<td>Squamous cell, esophagus</td>
</tr>
<tr>
<td>Squamous cell, vulva</td>
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</tbody>
</table>

High vs Low NK Cell Infiltration into Tumor

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


**TriKE™ for Treatment of Solid Tumor Cancers**

Significant reduction in solid tumor burden and improvement in survival after treatment with TriKE™

- TriKE™ has been evaluated in ovarian, breast, prostate, pancreatic ductal adenocarcinoma and lung cancer models.
- TriKE™ demonstrated significant reduction in tumor burden in animal models.
- TriKE™ increased overall survival in animal models of solid tumor cancers.
**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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