March 21, 2022

GT Biopharma Presents TriKE® Nanobody Pipeline (GTB-5550) Preclinical Multiple Myeloma Proof-of-Concept Data at 2022 EBMT Annual Meeting

- *GTB-5550 TriKE significantly enhances NK cell mediated killing of myeloma cells, even in the relatively low B7-H3-expressing H929 cell line*

- *Preclinical data demonstrates GTB-5550 reverses MDSC-induced myeloma growth*

BRISBANE, Calif., March 21, 2022 /PRNewswire/ -- GT Biopharma, Inc. ("the Company") (NASDAQ: GTBP), a clinical stage immuno-oncology company focused on developing innovative therapeutics based on the Company's proprietary tri-specific natural killer (NK) cell engager, TriKE® protein biologic technology platform, announced today, preclinical data to be presented at the hybrid 48th European Society for Blood and Marrow Transplantation Annual Meeting (EBMT). The poster presentation titled, "Tri-specific Killer Engager (TriKE®) against B7-H3 enhances NK cell mediated killing of multiple myeloma," is presented by Aimee Merino, MD, PhD, Assistant Professor of Medicine, Division of Hematology, Oncology and Transplantation at the University of Minnesota. GTB-5550 (B7-H3 TriKE) is the Company's tri-specific killer engager (TriKE) with camelid single-chain Fv fragments against B7-H3 (CD276) and CD16 linked by IL-15 to enhance NK cell killing of myeloma. GTB-5550 is part of GT Biopharma's portfolio of lead TriKE product candidates being investigated as a mono- and combination therapy against multiple myeloma.

Dr. Gregory Berk, President of R&D and Chief Medical Officer noted, "Testing GTB-5550

across several multiple myeloma cell-lines has yielded preclinical evidence suggesting further investigation of this TriKE in the clinic. We continue to push the boundaries of the natural killing power of NK cells enhanced by the Company's TriKE protein therapeutics across multiple types of liquid, solid and refractory cancer types. Additionally, this study further validates the potential of the Company's TriKE assets both as a mono- and combination therapy, with NK cells and anti-cancer agents."

Poster Title: "Tri-specific Killer Engager (TriKE®) against B7-H3 Enhances NK Cell Mediated Killing of Multiple Myeloma"

Background - Natural Killer (NK) cell-based therapies hold great promise in treating multiple myeloma. One method to enhance NK cell specificity against myeloma is antibody dependent cellular cytotoxicity through a CD16 receptor. B7-H3 (CD276) was targeted as its expression in myeloma is associated with decreased progression free survival, it exhibits low expression on healthy tissue, and it is expressed on myeloid derived suppressor cells (MDSC), which promote myeloma growth.

Study design and analysis – The study compared the ability of peripheral blood NK cells with or without GTB-5550 to kill myeloma cells in live imaging IncuCyte Zoom assays with escalating doses of TriKE. Maximal killing occurred with 3 nM concentration. Testing was performed across four different myeloma cell lines (H929, MM1S, RPMI-8226, U266). In the study, the efficacy of GTB-5550 was also tested in combination with the proteasome inhibitor bortezomib (10 nM) and the immunomodulatory drug lenalidomide (5 mM). Cytotoxicity curves were compared by repeated measures ANOVA and performed in triplicate.

Results **– NK cell mediated killing increased statistically significantly across all multiple myeloma cell lines tested. Combination therapy with GTB-5550 and anti-cancer agent showed enhanced killing as compared to NK cells or TriKE alone.**

Statistically significant increase in NK cell mediated killing across all lines when 3nM B7-H3-TriKE was added. Against U266 and MM1S, B7-H3-TriKE significantly enhanced killing at effector:target (E:T) ratios of 2:1 and 4:1. RPMI-8226 showed relatively high resistance to NK cell cytotoxicity but B7-H3-TriKE enhanced killing at E:T of 4:1. H929 cells were more potently killed in the presence of B7-H3-TriKE at E:T of 2:1 but there was no difference in killing at E:T 4:1 likely due to high natural cytotoxicity in both groups.

Combination therapy with GTB-5550, NK cells, and lenalidomide showed synergistic killing of H929 cells after 48 hours of live cell imaging ($p=0.047$) but combination with bortezomib did not further enhance killing as compared to NK cells and TriKE alone. Both lenalidomide and bortezomib showed a trend toward improved killing against MM1S when given with NK cells and B7-H3 TriKE but it did not reach statistical significance. Combination therapy with B7-H3-TriKE, NK cells, and lenalidomide or bortezomib showed synergistic killing of RPMI-8226 cells after 48 hours of live cell imaging ($p<0.001$ and 0.015 respectively). Bortezomib combined with GTB-5550 and NK cells enhanced killing in U266 cells ($p=0.037$).

Conclusion - B7-H3-TriKE significantly enhances NK cell mediated killing of myeloma cells, even in the relatively low B7-H3-expressing H929 line. Our data also shows it can reverse MDSC-induced myeloma growth.

The EBMT poster presentation details are as follows:

EBMT Poster Presentation Details

Title: A Tri-specific Killer Engager (TriKE) against B7-H3 enhances NK cell mediated killing of multiple myeloma
Abstract Number: AS-EBMT-2022-00508
Session: New Drugs- and Cell-Based Immune Therapies
Presentation Type: Poster
Session Date and Time: March 19, 2022 9:50 AM (CET)
Location: Prague Congress Center, Czech Republic
Poster Board Number: P153

Multiple Myeloma (Kahler's disease) -is a cancer of the plasma cell. Normal plasma cells are a type of white blood cell that helps make up your immune system. They are located within the bone marrow - the spongy interior of bones that produces blood cells. When your body is fighting an infection, plasma cells produce antibodies (proteins) which attack viruses and bacteria. If a plasma cell becomes cancerous, it multiplies rapidly. This is multiple myeloma. Malignant plasma cells may crowd out normal blood-forming cells within the bone marrow, reducing the production of healthy blood cells. Additionally, rather than producing infection-fighting antibodies, the cancer cells begin to produce an abnormal antibody called a monoclonal protein (m protein) or paraproteins. In the urine, they are called Bence Jones proteins. These proteins do not fight against infection. For more information about multiple myeloma please click here.

About GT Biopharma, Inc.

GT Biopharma, Inc. is a clinical stage biopharmaceutical company focused on the development and commercialization of immuno-oncology therapeutic products based on our proprietary TriKE® NK cell engager platform. Our TriKE® platform is designed to harness and enhance the cancer killing abilities of a patient's immune system's natural killer cells. GT Biopharma has an exclusive worldwide license agreement with the University of Minnesota to further develop and commercialize therapies using TriKE® technology. For more information, please visit gtbiopharma.com.

Forward-Looking Statements

Certain statements in this press release may constitute "forward-looking statements" regarding future events and our future results. All statements other than statements of historical facts are statements that could be deemed to be forward-looking statements. These statements are based on current expectations, estimates, forecasts, and projections about the markets in which we operate and the beliefs and assumptions of our management. Words such as "expects," "anticipates," "targets," "goals," "projects", "intends," "plans," "believes," "seeks," "estimates," "endeavors," "strives," "may," or variations of such words, and similar expressions are intended to identify such forward-looking statements. Readers are cautioned that these forward-looking statements are subject to a number of risks, uncertainties and assumptions that are difficult to predict, estimate or verify. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. Such risks and uncertainties include those factors described in our most

recent annual report on Form 10-K, as such may be amended or supplemented by subsequent quarterly reports on Form 10-Q, or other reports filed with the Securities and Exchange Commission. Readers are cautioned not to place undue reliance on these forward-looking statements. The forward-looking statements are made only as of the date hereof, and we undertake no obligation to publicly release the result of any revisions to these forward-looking statements. For more information, please refer to our filings with the Securities and Exchange Commission.

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