December 8, 2021

# GT Biopharma Demonstrates Novel B7-H3 Targeting Dual Camelid Nanobody BiKE and GTB-5550 Induce NK Cell Activation Against Broad Spectrum of Tumors at ESMO IO Congress 2021

### - GTB-5550, which harbors wild-type IL-15, and BiKE display broad activity against B7-H3-expressing tumors

### - Compared to monomeric IL-15, GTB-5550 shows CD16-dependent metabolic activation of NK cells

BEVERLY HILLS, Calif., Dec. 8, 2021 /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 natural killer (NK) cell engager, TriKE® protein biologic technology platform, today announced that the Company's mini-poster presentation abstract is now broadly available on the European Society for Medical Oncology ("ESMO") Immuno-Oncology ("IO") Congress 2021 abstracts webpage. The congress is being held from December 8-11, 2021, in Geneva Switzerland.

"B7-H3 is a checkpoint molecule under intense investigation as an immune therapy target for solid and hematologic tumors. These proof of concept data via in vivo animal models validates GTB-5550's candidacy for further investigation, noted Dr. Gregory Berk, President of R&D, Chief Medical Officer and Interim Chief Executive Officer. GT BioPharma's diverse

but focused pipeline of TriKE® Nanobodies are highly targeted natural killer cell engagers, resulting in potent activation, proliferation, and persistence of the patient's NK cells, without activation of T-cells, which are often responsible for the side effects of T-cell directed therapies. As such, we look forward to continuing the Company's progress in the new year including the advancement of GTB-3650, second-generation TRIKE® for patients with relapsed/refractory Acute Myelogenous Leukemia (AML) and high-risk Myelodysplastic Syndrome (MDS)."

The study was conducted by Dr. Jeff Miller's lab, University of Minnesota where functional assays were conducted with various ovarian, prostate, and hematologic malignancy cell lines with varying levels of B7H3 expression from none to very high levels. Dr. Miller's lab previously showed that dual camelid nanobody tri-specific killer engager (TriKE) (GTB-5550) specifically bound B7-H3 on PC3/C4-2 prostate cancer (PCa) cells and activated peripheral blood (PB) NK cells. We have since developed a dual camelid bispecific killer engager (BiKE) targeting B7-H3 and show that both GTB-5550, which harbors wild-type IL-15, and BiKE display broad activity against B7-H3-expressing tumors. Compared to monomeric IL-15, GTB-5550 shows CD16-dependent metabolic activation of NK cells.

**Presentation highlights from the mini-poster titled, *"Novel B7-H3 Targeting Dual-Nanobody NK Cell Engagers Display Robust Activity"* include:**

- Study Background
  - BiKE and GTB-5550 were manufactured in a mammalian expression system and purified from supernatants.
  - Models were used to evaluate how the BiKE and GTB-5550 induce NK cell degranulation (CD107a) and interferon gamma production through a variety of cell lines including PCa cells harboring enzalutamide resistance with divergent mechanisms including 22RV1 (androgen ligand-independent AR-V7 splice variant) as well as a spontaneously resistant LNCaP model (AR hyper activation), as well as a CREB5 overexpressing (epithelial to mesenchymal transition) LNCaP model.
  - Metabolic stimulation was measured in NK-92 cell lines.
  - PB NK cells were robustly activated, compared to controls, when treated with GTB-5550 or BiKE and cultured with enzalutamide resistant PCa, osteosarcoma (U2OS, SaOS2), rhabdomyosarcoma (RH30), ovarian carcinoma (MA148, OVCAR8), AML (MV4;11, THP-1) and multiple myeloma (MM1S) cell lines.
  - GTB-5550 was approximately 2 times more potent than NCI IL-15 in terms of metabolic stimulation of CD16+ NK-92 cells, but not CD16- NK-92 cells. Spheroid killing assays and deeper metabolic analyses are in progress.
- Results of the Study
  - The data demonstrated that the novel dual camelid nanobody BiKE and GTB-5550 induce NK cell activation against a broad spectrum of tumors expressing B7-H3. Furthermore, B7-H3 is expressed at high levels on prostate cancer cell lines demonstrating enzalutamide resistance, thus inducing efficient targeting of these therapy PCa refractory lines. This B7-H3 targeting NK platform demonstrates broad translational potential. GMP production of GTB-5550 has been initiated.

**ESMO IO 2021 presentation details**

**e-Poster Display Title (#126P):** *Novel B7-H3 targeting dual nanobody NK cell engagers display robust activity against a broad spectrum of solid and hematologic malignancies*

The full abstract has been published on ESMO-IO website and the Company has published the poster on the company's website in the "Presentations" section of its corporate website.

For event details please visit: https://www.esmo.org/meetings/esmo-immuno-oncology-congress-2021/programme

**About Camelid Antibodies**

*Camelid antibodies* are single domain antibodies (sdAbs) from the Camelidae family of mammals that include llamas, camels, and alpacas. These animals produce 2 main types of antibodies. One type of antibody camelids produce is the conventional antibody that is made up of 2 heavy chains and 2 light chains. They also produce another type of antibody that is made up of only 2 heavy chains and no light chain. This is known as heavy chain IgG (hcIgG). While these antibodies do not contain the CH1 region, they retain an antigen binding domain called the VHH region. VHH antibodies, also known as single domain antibodies, contain only the VHH region from the camelid antibody. Camelid antibodies have key characteristics, which include high affinity and specificity (equivalent to conventional antibodies), high thermostability, good solubility and strictly monomeric behavior, small size, relatively low production cost, ease of genetic engineering, format flexibility or modularity, low immunogenicity, and a higher penetration rate into tissues.

**About GTB-5550**

GTB-5550 TriKE® product candidate is being developed for the treatment of B7H3+ solid tumor cancers. GTB-5550 is a single-chain, tri-specific scFv recombinant fusion protein conjugate composed of the variable regions of the heavy and light chains of anti-CD16 and anti-B7H3 antibodies and human IL-15.

**About GTB-3650**

GTB-3650 is the Company's lead second-generation Tri-Specific Killer Engager TriKE® program currently in preclinical development for the treatment of relapsed/refractory acute myelogenous leukemia (AML) and high-risk myelodysplastic syndrome (MDS).

**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**

This press release contains certain forward-looking statements that involve risks,

uncertainties and assumptions that are difficult to predict, including statements regarding our clinical focus, and our current and proposed trials. Words and expressions reflecting optimism, satisfaction or disappointment with current prospects, as well as words such as "believes", "hopes", "intends", "estimates", "expects", "projects", "plans", "anticipates" and variations thereof, or the use of future tense, identify forward-looking statements, but their absence does not mean that a statement is not forward-looking. Our forward-looking statements are not a guarantee of performance, and actual results could differ materially from those contained in or expressed by such statements. In evaluating all such statements, we urge you to specifically consider the various risk factors identified in 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 September 30, 2021, and our other filings with the Securities and Exchange Commission, any of which could cause actual results to differ materially from those indicated by our forward-looking statements.

Our forward-looking statements reflect our current views with respect to future events and are based on currently available financial, economic, scientific, and competitive data and information on current business plans. You should not place undue reliance on our forward-looking statements, which are subject to risks and uncertainties relating to, among other things: (i) the sufficiency of our cash position and our ongoing ability to raise additional capital to fund our operations, (ii) our ability to complete our contemplated clinical trials, or to meet the FDA's requirements with respect to safety and efficacy, (iii) our ability to identify patients to enroll in our clinical trials in a timely fashion, (iv) our ability to achieve approval of a marketable product, (v) design, implementation and conduct of clinical trials, (vii) the results of our clinical trials, including the possibility of unfavorable clinical trial results, (vii) the market for, and marketability of, any product that is approved, (viii) the existence or development of treatments that are viewed by medical professionals or patients as superior to our products, (ix) regulatory initiatives, compliance with governmental regulations and the regulatory approval process, and social conditions, and (x) various other matters, many of which are beyond our control. Should one or more of these risks or uncertainties develop, or should underlying assumptions prove to be incorrect, actual results may vary materially and adversely from those anticipated, believed, estimated, or otherwise indicated by our forward-looking statements.

We intend that all forward-looking statements made in this press release will be subject to the safe harbor protection of the federal securities laws pursuant to Section 27A of the Securities Act, to the extent applicable. Except as required by law, we do not undertake any responsibility to update these forward-looking statements to take into account events or circumstances that occur after the date of this press release. Additionally, we do not undertake any responsibility to update you on the occurrence of any unanticipated events which may cause actual results to differ from those expressed or implied by these forward-looking statements.

TriKE® is a registered trademark owned by GT Biopharma, Inc.

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