December 6, 2018

GT Biopharma Presents Positive Preclinical Data of Tri-specific NK Cell Engager (TriKE) at the 60th American Society of Hematology (ASH) Annual Meeting & Exposition

– Company's proprietary TriKE product candidates have the potential to serve as a relatively safe, cost-effective, and easy-to-use therapy for refractory/relapsed AML, high-risk MDS and advanced systemic mastocytosis –

– Positive preclinical findings highlight the clinical potential of the CLEC12A TriKE individually or in combination with the CD33 TriKE for the treatment of MDS and AML –

– Company to commence first-in-human Phase 1 study with its first-in-class TriKE, for the treatment of AML, MDS and mastocytosis –

LOS ANGELES, Dec. 06, 2018 (GLOBE NEWSWIRE) -- GT Biopharma, Inc. (OTCQB: GTBP and Euronext Paris GTBP.PA) ("GT Biopharma" or the "Company"), an immuno-oncology biotechnology company focused on innovative treatments based on the Company's proprietary NK-engager and Bispecific Antibody Drug Conjugate platforms, announced today that it presented data demonstrating the effectiveness of the Company's Tri-specific Killer Engagers (TriKEs) for the treatment of acute myeloid leukemia (AML) presented at the American Society of Hematology (ASH) Annual Meeting.

Jeffrey Miller, MD, Deputy Director, Masonic Cancer Center, University of Minnesota commented, "These studies demonstrate the adaptability of the TriKE platform to optimize TriKE constructs and candidate selection in order to address unmet medical needs. We continue to work with our partners at GT Biopharma in moving the TriKE platform forward."

The Company's TriKE product candidates are single-chain, tri-specific scFv recombinant fusion proteins composed of the variable regions of the heavy and light chains (or heavy chain only) of anti-CD16 antibodies, wild-type or a modified form of IL-15 and the variable regions of the heavy and light chains of an antibody designed to precisely target a specific tumor antigen. GT Biopharma utilizes the NK stimulating cytokine human IL-15 as a crosslinker between the two scFvs which is designed to provide a self-sustaining signal leading to the proliferation and activation of NK cells thus enhancing their ability to kill cancer cells mediated by antibody-dependent cell-mediated cytotoxicity (ADCC). GT Biopharma has an exclusive worldwide license agreement with the University of Minnesota to further develop and commercialize cancer therapies using proprietary TriKE technology developed

by researchers at the university to target NK cells to cancer.

“We continue to be encouraged by the data from our Trike program being conducted by leading NK cell experts at the University of Minnesota. These findings have supported us with the confidence to proceed with our first-in-class TriKE, Phase 1 study,” commented Raymond Urbanski, M.D., Ph.D., Chief Executive Officer of GT Biopharma. “We are grateful to renowned NK cell expert, Jeffrey Miller, MD, Deputy Director, Masonic Cancer Center, University of Minnesota and his team, and look forward to providing further updates as we continue to advance what we believe to be a potentially revolutionary product candidate.”

Graduate student, Upasana Sunil Arvindam, MSc, BSc, working with Drs. Miller and Felices at the University of Minnesota, presented the abstract titled, “*CD16-IL15-CLEC12A Tri-specific Killer Engager (TriKE) Drives NK Cell Expansion, Activation, and Antigen Specific Killing of Cancer Stem Cells in Acute Myeloid Leukemia*,” as part of the Acute Myeloid Leukemia: Novel Therapy, Excluding Transplantation: Poster I session at ASH. To access the presented poster, click here.

For the preclinical study, Dr. Arvindam and her team developed a 1615CLEC12A TriKE molecule to target AML cells using Natural Killer (NK) cells. This molecule contains an anti-CD16 camelid nanobody to activate NK cells, an anti-CLEC12A single chain variable fragment (scFv) to engage cancer targets, and an IL-15 molecule that drives NK cell priming, expansion and survival.

The CLEC12A TriKE was developed in a mammalian cell system to ensure that appropriate post-translational modifications are present. The researchers confirmed that the TriKE binds specifically to HL-60 and THP-1 target cells that express CLEC12A compared to Raji cells that do not express CLEC12A. Treatment of peripheral blood mononuclear cells (PBMCs) with the CLEC12A TriKE drives a significant increase in NK cell specific proliferation over 7 days as measured by Cell Trace dilution compared to treatment with a CLEC12A scFv or IL-15 alone (69.7 ± 6.7% vs 11.9 ± 2.5% vs 38.4 ± 7.3%). In these assays, the efficacy of the CLEC12A TriKE was comparable to the CD33 TriKE. The data demonstrates that the CLEC12A TriKE drives NK cell specific proliferation, degranulation, cytokine secretion, and killing of tumor targets *in vitro*. Apart from AML, CLEC12A is expressed on cancer cells and LSCs in patients with myelodysplastic syndromes (MDS).

The presented preclinical findings highlight the clinical potential of the CLEC12A TriKE individually or in combination with the CD33 TriKE for the treatment of MDS and AML and ultimately led to the establishment of a first-in-human Phase 1 study with GTB-3550 (OXS-3550), its first-in-class (TriKE), for the treatment of AML, MDS and mastocytosis, which GT Biopharma recently announced. The study will be led by Principal Investigator, Sarah A. Cooley, MD, MS, Associate Professor, Division of Hematology, Oncology and Transplantation at Masonic Cancer Center, University of Minnesota.

The abstract titled, “*Induced Pluripotent Stem Cell-Derived NK Cells Genetically Modified to Express NKG2C/DAP12 Mediate Potent Function When Targeted through an NKG2C/IL-15/CD33 Tri-Specific Killer Engager (TriKE)*,” was presented in an oral presentation by graduate student Emily Chiu, PhD, Medical School, University of Minnesota. To access the presentation slides, click here.

Having demonstrated stable expression and intact signaling of NKG2C/DAP12 in iNK cells,

Dr. Chiu and her team next created a TriKE molecule with single chain Fv fragments specific for NKG2C (on iNK cells) and CD33 (on AML cells), as well as IL15 (to support iNK cell survival and proliferation). Without the addition of NKG2C/CD33/IL15 TriKE, the frequencies of both NKG2C iNK cells and NKG2C/DAP12 iNK cells producing IFNg was relatively low (< 10%). Addition of NKG2C/IL15/CD33 TriKE in the assay markedly increased the frequency of IFNg production by both NKG2C iNK cells (19.1%) and NKG2C/DAP12 iNK cells (25.8%). Finally, the team directly tested the ability of the NKG2C/IL15/CD33 TriKE molecule to trigger target killing by engineered iNK cells monitored over a 24hour period. THP1 target cells were dye labeled and plated in wells with either NKG2C iNK cells or NKG2C/DAP12 iNK cells at a 5:1 effector-to-target ratio with or without NKG2C/CD33/IL15 TriKE. The researchers found that in the absence of TriKE, there was no killing of THP1 targets. In contrast, both NKG2C iNK cells and NKG2C/DAP12 iNK cells mediated robust THP1 killing with the addition of NKG2C/CD33/IL15 TriKE, with NKG2C/DAP12 iNK cells exhibiting the strongest response.

Results from the study provided a proof-of-concept that iNK cells engineered to express NKG2C/DAP12 can be used in combination with a novel NKG2C/IL15/CD33 TriKE molecule to effectively target cancer cells. Engaging NK cells through NKG2C, restricted to adaptive NK cells or genetically modified iPSC will be more specific than CD16, which will bind to CD16A on NK cells but also have off-target binding to CD16B on neutrophils. Because of the enormous expansion and engineering capacity of the iNK cell platform, the Company believes it is in a unique position to create an “off-the-shelf” NK cellular therapy that is targeted, specific and efficacious.

About Acute Myelogenous Leukemia (AML)

AML is the most common form of adult leukemia with 21,000 new cases expected in 2018 alone, according to the American Cancer Society. AML patients typically receive frontline therapy, most commonly chemotherapy, which includes cytarabine and an anthracycline, a therapy that has not changed in over 40 years. However, there remains a significant unmet need in these therapies with about half of AML patients experiencing relapses or requiring alternative therapies. The Company is developing GTB-3550 to serve as a relatively safe, cost-effective, and easy-to-use therapy for resistant/relapsing AML and could also be combined with chemotherapy as frontline therapy thus targeting the larger patient population.

About GT Biopharma, Inc.

GT Biopharma, Inc. is a clinical stage biopharmaceutical company focused on the development and commercialization of immuno-oncology products based off our proprietary Tri-specific Killer Engager (TriKE), Tetra-specific Killer Engager (TetraKE) and bi-specific Antibody Drug Conjugate (ADC) technology platforms. Our TriKE and TetraKE platforms generate proprietary moieties designed to harness and enhance the cancer killing abilities of a patient's own natural killer, or NK, cells. Once bound to a NK cell, our moieties are designed to enhance the NK cell and precisely direct it to one or more specifically-targeted proteins (tumor antigens) expressed on a specific type of cancer, ultimately resulting in the cancer cell's death. TriKEs and TetraKEs are made up of recombinant fusion proteins, can be designed to target certain tumor antigens on hematologic malignancies, sarcomas or solid tumors and do not require patient-specific customization. They are designed to be

dosed in a common outpatient setting similar to modern antibody therapeutics and are expected to have reasonably low cost of goods. Our ADC platform can generate product candidates that are bi-specific, ligand-directed single-chain fusion proteins that, we believe, represent the next generation of ADCs.

For more information, please visit www.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 guarantees 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 Form 10-K for the fiscal year ended December 31, 2017 in the section titled "Risk Factors" in Part I, Item 1A and in our subsequent 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 Phase 1 study of TriKe, GTB-3550 and or our Phase 2 trial of CTB-1550 and 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.

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