April 11, 2022

GT Biopharma Presents Preclinical Data Demonstrating Novel B7H3+ Tumor Targeting GTB-5550 TriKE® Driving NK Cell Activation and ADCC Against Head and Neck Squamous Cell Carcinomas at AACR Annual Meeting 2022

- Ongoing experiments will evaluate the functionality and efficacy of the B7H3 TriKE in vivo
- Future studies will also involve assessments of the B7H3 TriKE efficacy in the HNSCC tumor microenvironment

BRISBANE, Calif., April 11, 2022 (GLOBE NEWSWIRE) -- 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 that it is presenting pre-clinical data at the American Association For Cancer Research Annual Meeting 2022. The poster presentation titled, "#3435: GTB-5550 (cam16-IL15-camB7H3) Tri-specific Killer Engager (TriKE®) Drives NK Cell Activation and ADCC against Head and Neck Squamous Cell Carcinomas," presented by Dr. Jeff Miller's laboratory, University of Minnesota.

GTB-5550 is the Company's B7H3-targeted tri-specific killer engager (TriKE) and is part of GT Biopharma's portfolio of TriKE product candidates being investigated in several preclinical models against a broad class of solid tumor cancers. Structurally, GTB-5550 TriKE consists of a humanized camelid nanobody against CD16, a camelid nanobody against B7H3 and a wild type IL-15 sequence between the two engagers, and it functions by bridging the NK and tumor cells.

Dr. Gregory Berk, President of R&D and Chief Medical Officer noted, "B7H3 is a novel immune checkpoint of the B7 family and is highly expressed on a variety of human cancers including but not limited to head and neck cancers, melanoma, ovarian cancer, prostate cancer, and brain cancer. Our work with GTB-5550 along with our other lead pipeline asset (GTB-3650) demonstrate remarkable promise in preclinical studies as potential new immunotherapies with high specificity towards targeted cancer cells but not healthy tissue where these immune checkpoint inhibitors are not highly expressed or absent."

Poster Title - "#3435: GTB-5550 (cam16-IL15-camB7H3) Tri-specific Killer Engager

(TriKE®) Drives NK Cell Activation and ADCC against Head and Neck Squamous Cell Carcinomas"

Background - According to the American Society of Clinical Oncology's information hub, head and neck cancers account for about 4% of all cancers in the United States. In 2021, an estimated 66,630 people (48,740 men and 17,890 women) will develop head and neck cancer. In some settings, like Fanconi anemia (FA), patients receive curative treatments (allogeneic stem cell transplantation), only to develop HNSCC in early adulthood at a high rate of incidence. Current treatment strategies for non-FA HNSCC patients include surgery, chemotherapy and radiotherapy. However, these are not viable treatment options for FA HNSCC patients due to their low tolerance for the high toxicity levels of chemotherapy and radiation. Therefore, there is a critical need for novel and targeted therapeutic interventions for the treatment of FA HNSCC patients.

Study Design and Analysis - B7H3, a checkpoint member of the B7 and CD28 families, is overexpressed on several solid tumors but is absent or not expressed on healthy tissues. It is a promising target for immunotherapy, and recent basket trials, particularly in prostate cancer, have demonstrated strong clinical signals. Here we developed and tested the ability of GTB-5550, a tri-specific killer engager (TriKE) that includes a B7H3 targeting component, to direct NK cell killing to B7H3-expressing Head and Neck cancer targets. This TriKE molecule includes an NK cell engaging domain containing a humanized camelid nanobody against CD16, a camelid nanobody against B7H3 and a wild type IL-15 sequence between the two engagers. We assessed B7H3 expression by flow cytometry of wild-type HNSCC cells and a paired version with a CRISPER KO of the FANCA gene and determined that the KO had no effect on B7H3 expression. Thus, GTB-5550 activity against HNSCC should be present on both normal HNSCC and FA-HNSCC settings.

NK cell responses against HNSCC lines in the presence of GTB-5550 were assessed through either flow cytometry based functional assays, to evaluate NK cell degranulation and cytokine secretion, or IncuCyte imaging assays, to directly assess target killing.

Results - NK cell degranulation and IFN-gamma production of GTB-3550-treated samples were higher compared to that of control samples treated with B7H3 single domain or IL-15 alone. GTB-5550 also induced more HNSCC target cell killing by NK cells compared to treatment with the B7H3 single domain or IL-15 alone irrespective of the FANCA gene, both in 2D and 3D IncuCyte imaging assays.

Conclusions - There is a critical need for a targeted therapy that can effectively eliminate HNSCC cells while sparing healthy cells. Treatment with the B7H3 TriKE effectively induces NK cell degranulation and cytokine production against HNSCC, as well as drives targeted killing of HNSCC in vitro. Taken together, this data demonstrates that GTB-5550 is able to drive NK cell activity against B7H3- expressing HNSCC cells, which presents potential for a B7H3-targeted TriKE to be used clinically to treat HNSCC or FA-HNSCC patients. Ongoing experiments will evaluate the functionality and efficacy of the B7H3 TriKE in vivo. Future studies will involve assessments of the B7H3 TriKE efficacy in the HNSCC tumor microenvironment in addition to evaluating whether HPV status of HNSCC has any implications on efficacy of the TriKE in the HNSCC tumor microenvironment as previous studies have reported differential NK cell activity in HPV+/- HNSCC tumor microenvironment.

AACR Annual Meeting 2022 Poster Details:

Title: GTB-5550 (cam16-IL15-camB7H3) Tri-specific Killer Engager (TriKE®) drives natural killer cell activation and ADCC against head and neck squamous cell carcinomas
Abstract Number: Abstract control number 3334, permanent abstract number 3435
Session: Clinical Research Excluding Trials, Combination Immunotherapies / Therapeutic Antibodies
Presentation Type: Poster
Session Date and Time: April 12, 2022 1:30 PM – 5:00 PM
Location: Ernest N. Morial Convention Center, Exhibit Halls D-H, Poster Section 32, New Orleans
Poster Board Number: 16

About Squamous Cell Carcinomas of the Head and Neck -Cancers that are known collectively as head and neck cancers usually begin in the squamous cells that line the mucosal surfaces of the head and neck (for example, those inside the mouth, throat, and voice box). These cancers are referred to as squamous cell carcinomas of the head and neck. Head and neck cancers can also begin in the salivary glands, sinuses, or muscles or nerves in the head and neck, but these types of cancer are much less common than squamous cell carcinomas. For more information about squamous cell carcinomas of the head and neck 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.

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

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