March 9, 2022

GT Biopharma Presented Preclinical Data Demonstrating Novel Mesothelin-Targeted TriKE® Driving Cytotoxicity Across All Stages of Non-Small Cell Lung Cancer at ESMO TAT 2022

- Results suggest that mesothelin-targeted TriKE can work alongside current standard of care and provide benefit even in the hypoxic environment of a solid tumor

BRISBANE, Calif., March 9, 2022 /PRNewswire/ -- GT Biopharma, Inc. (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, presented preclinical data demonstrating its novel TriKE driving NK cell immunotherapy against non-small cell lung cancer (NSCLC) in the hypoxic solid tumor microenvironment at ESMO's Targeted Anticancer Therapies Congress (TAT).

Gregory Berk, M.D., the Company's President of R&D and Chief Medical Officer noted, "This pre-clinical evidence suggests, despite the difference in circulating immune cells of Stage IVB NSCLC patients, a mesothelin-targeted TriKE can work alongside current standard of care and provide benefit even in the hypoxic environment of a solid tumor, meriting further investigation of this novel, targeted TriKE."

Driving NK cell immunotherapy against NSCLC, in the context of hypoxia, using Tri-specific Killer Engager (TriKE®)

Background - Currently, Tri-specific killer engagers (TriKE®) are being tested in the clinic to treat leukemia and lymphoma. These TriKE's cross-link CD16/FcγRIII and the tumor antigen on NK cells which drives cytotoxicity while IL15 provides survival and proliferation signals to NK cells. Mesothelin (MSLN), is currently a tumor antigen being targeted in various cancers including NSCLC. The current study conducted by Dr. Jeff Miller's laboratory, University of Minnesota, evaluated whether a MSLN-targeted TriKE could drive cytotoxicity towards NSCLC cells at all stages of disease in the presence of hypoxia, a challenge in the NSCLC tumor microenvironment.

Study design and analysis - Using peripheral blood mononuclear cells (PBMC) collected from NSCLC patients, (1) before patients started standard treatment, (2) after initial treatment and (3) at disease progression where applicable. The study challenged patient PBMC with a NSCLC cell line (NCI-H460) for 5 hours in the presence of monensin and brefeldin A, measuring degranulation (CD107a) and cytokine production (IFNγ) by flow cytometry (live, single CD56+/CD3- cells). Compared to NK cells alone (NT); NK cells alone with drug ('TriKE'); or NK cells with tumor alone.

Results

NSLC have altered NK cells - Differential abundance analysis of immune subsets in early stage or late stage patient groups were performed using Astrolabe Diagnostics software. The TriKE was able to induce significant ($p<0.0001$) activity against H460 cells for both groups. The analysis revealed a greater abundance of CD56+/CD16+ NK cells and fewer CD33+/CD14- myeloid cells in early stage patients compared to late stage patients before treatment onset. The lack of CD16, which drives cytotoxicity, and the abundance of myeloid cells, that can suppress NK cell function, suggested late stage NSCLC patients may respond differently to biologics targeting NK cell cytotoxicity.

Mesothelin-targeted TriKE drives NK cell function regardless of disease stage and at all stages of treatment: While hypoxia impairs NK cell cytotoxicity, the study's MSLN-targeted TriKE enhanced NK cell cytotoxicity of lung cancer cells (H460) after exposure to hypoxia for 7 days, during exposure to hypoxia and in the assay itself. The data demonstrated that TriKE induced degranulation and cytokine production in patient NK cells when in the presence of tumor cells (H460) at all stages of treatment (before treatment, after initial treatment and at progression).

Conclusion - This pre-clinical evidence suggests, despite the difference in circulating immune cells of Stage IVB NSCLC patients, mesothelin-targeted TriKE can work alongside current standard of care and provide benefit even in the hypoxic environment of a solid tumor.

The ESMO poster presentation details are as follows:

ESMO Targeted Anticancer Therapies Congress (TAT)
Title: Driving NK cell immunotherapy against NSCLC, in the context of hypoxia, using Tri-specific Killer Engager (TriKE®)
Abstract Number: 250
Session: Immunotherapy

Presenter: Jeff Miller, M.D., Consulting Chief Scientific Officer, University of Minnesota
Presentation Type: Poster
Session Date and Time: March 7, 9:20 AM (CET) (On-demand e-poster display)
Location: Virtual
Poster Board Number: 17P

The presentation was published on the ESMO website. It is also available on the GT Biopharma website: https://www.gtbiopharma.com/news-media/presentations.

Non-small cell lung cancer (NSCLC) is any type of epithelial lung cancer other than small cell lung cancer (SCLC). Non-small cell lung cancer (NSCLC) is a disease class including squamous cell carcinoma (25% of lung cancers), adenocarcinoma (40% of lung cancers), and large cell carcinoma (10% of lung cancers) in which malignant cancer cells form in the tissues of the lung. For more information about NSCLC 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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