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# GT Biopharma Receives FDA Clearance to Commence First-in-Human Phase 1 Study of its First-in-Class Tri-Specific Killer Engager (TriKE), GTB-3550, for the Treatment of Acute Myelogenous Leukemia, Myelodysplatic Syndrome and Mastocytosis

LOS ANGELES, Nov. 01, 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 its Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) is now open and it is authorized to initiate a first-in-human Phase 1 study with GTB-3550 (OXS-3550), its first-in-class (TriKE), for the treatment of acute myelogenous leukemia (AML), myelodysplatic syndrome (MDS) and mastocytosis. 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.

“GTB-3550 is a protein immune engager that binds to natural killer (NK) cells and targets them specifically to leukemia cells,” said renowned NK cell expert, Jeffrey Miller, MD, Deputy Director, Masonic Cancer Center, University of Minnesota. “Our team has been working on the optimal construct for years and we are excited to see it is ready for clinical testing. In addition, the same TriKE protein will deliver an interleukin-15 stimulus, a growth factor that makes NK cells proliferate and be more active.”

“The clinical trials team at the University of Minnesota is excited to commence the Phase 1 trial testing this novel immunotherapeutic agent, GTB-3550,” said Dr. Cooley. “Building on over a decade of successful trials using NK cell infusions from related donors to kill tumors, Masonic Cancer Center researchers designed this protein to activate a patient’s own NK cells and, importantly, to direct them to specifically kill CD33+ tumor cells. The pre-clinical data are extraordinarily compelling, and success with GTB-3550 in this study will allow us to

develop a broad pipeline of TriKE agents against different tumor targets."

This single center, first-in-human Phase 1 clinical trial of GTB-3550 will enroll up to 60 subjects with CD33-expressing high risk for refractory/relapsed AML, MDS, or advanced systemic mastocytosis. Subjects will receive a single course of GTB-3550 TriKE given as 3 weekly treatment blocks. Each block consists of four consecutive 24-hour continuous infusions of GTB-3550 TriKE followed by a 72-hour break after Block #1 and #2. Disease response will be assessed by bone marrow biopsy performed between Day 21 and Day 42 after the start of the 1st infusion. Follow-up for response and survival continues through 6 months from treatment start. The primary objective from the Phase 1 dose finding portion of the study will be to identify the maximum tolerated dose (MTD) of GTB-3550 TriKE defined as the dose level that most closely corresponds to a dose limiting toxicity rate (DLT) of 20%. The primary objective from the Phase 2 extended portion of the study will be the potential efficacy of GTB-3550 TriKE, measured using rates of complete and partial remission. Subjects experiencing clinical benefit and no unacceptable side effects may be considered for a 2nd course of GTB-3550 TriKE on a compassionate basis.

"The opening of this IND allows us to proceed with our first-in-class TriKE, Phase 1 study and importantly, marks a significant step forward in our clinical development strategy of our potentially revolutionary product candidate," commented Raymond Urbanski, M.D., Ph.D., Chief Executive Officer of GT Biopharma. "We are privileged to be advancing this program with the world's leading experts in NK cell-based therapy."

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.

**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 Myelodysplastic Syndrome (MDS)**

Myelodysplastic syndromes (MDS) are conditions that can occur when the blood-forming cells in the bone marrow become abnormal, leading to low numbers of one or more types of blood cells. There are several different types of MDS, based on how many types of blood cells are affected and other factors, although the most common finding in MDS is a shortage of red blood cells (anemia). The number of people with MDS diagnosed in the U.S. each year is estimated to be ~10,000. MDS is uncommon before age 50 and is most commonly diagnosed in people in their 70s. In about 1 in 3 patients, MDS can progress to AML, a rapidly growing cancer of bone marrow cells.

**About Mastocytosis**

Mastocytosis is a rare disorder characterized by abnormal accumulations of mast cells in the skin, bone marrow, and internal organs (liver, spleen, gastrointestinal tract and lymph nodes). Cases beginning during adulthood tend to be chronic and involve the bone marrow in addition to the skin, whereas, during childhood, the condition is often marked by skin manifestations with no internal organ involvement and can often resolve during puberty. In most adult patients, mastocytosis tends to be persistent, and may progress into a more advanced category in a minority of patients. Mastocytosis affects both males and females and can begin during childhood or adulthood. In children, 80% of cases appear during the first year of life, and the majority is limited to the skin. Adults who develop mastocytosis more often have systemic forms of the disease. Cutaneous forms of the disease account for less than 5% of adult cases. An estimate of prevalence from a recent population-based study is approximately 1 case per 10,000 people.

**About GTB-3550**

GTB-3550 (OXS-3550) is the Company's first Tri-specific Killer Engager (TriKE) product candidate being initially developed for the treatment AML. GTB-3550 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-CD33 antibodies and a modified form of IL-15. When the NK stimulating cytokine human IL-15 is used as a crosslinker between the two scFvs, it provides a self-sustaining signal that activates NK cells and enhances their ability to kill. We intend to study this anti-CD16-IL-15-anti-CD33 tri-specific killer engager, or TriKE, in CD33 positive leukemias, a marker expressed on tumor cells in AML, myelodysplastic syndrome, or MDS, and other hematopoietic malignancies. CD33 is primarily a myeloid differentiation antigen with endocytic properties broadly expressed on AML blasts and, possibly, some leukemic stem cells. CD33 or Siglec-3 (sialic acid binding Ig-like lectin 3, SIGLEC3, SIGLEC3, gp67, p67) is a transmembrane receptor expressed on cells of myeloid lineage. It is usually considered myeloid-specific, but it can also be found on some lymphoid cells. The anti-CD33 antibody fragment that will be used for these studies was derived from the M195 humanized anti-CD33 scFV and has been used in multiple human clinical studies. It has been exploited as target for therapeutic antibodies for many years. Improved survival seen in many patients when the antibody-drug conjugate gemtuzumab was added to conventional chemotherapy validates this approach. GT Biopharma believes that GTB-3550 could 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**

Except for historical information contained herein, the statements in this release are forward-looking and made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are inherently unreliable and actual results may differ materially. Examples of forward-looking statements in this news release include statements regarding the payment of dividends, marketing and distribution plans, development activities and anticipated operating results. Factors which could cause actual results to differ materially from these forward-looking statements include such factors as the Company's ability to accomplish its business initiatives, significant fluctuations in marketing expenses and ability to achieve and expand significant levels of revenues, or recognize net income, from the sale of its products and services, as well as the introduction of competing products, or management's ability to attract and maintain qualified personnel necessary for the development and commercialization of its planned products, and other information that may be detailed from time to time in the Company's filings with the United States Securities and Exchange Commission. The Company undertakes no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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