G1 Therapeutics Initiates Phase 2 Trial to Support the Antitumor Mechanism of Action (MOA) of Trilaciclib in the Tumor Microenvironment

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New Trial Designed to Further Investigate the Immune-Based MOA of Trilaciclib and Help Determine Future Target Tumor Types and Treatment Combinations

RESEARCH TRIANGLE PARK, N.C., Dec. 01, 2021 (GLOBE NEWSWIRE) -- G1 Therapeutics, Inc. (Nasdaq: GTHX), a commercial-stage oncology company, today announced that the Company has initiated a Phase 2, single arm, open-label study of trilaciclib in patients with early-stage triple negative breast cancer (TNBC) designed to further investigate the role of trilaciclib in modulating the anti-tumor immune response. Pathologic complete response endpoints are also being evaluated in this trial. Initial results of this study are expected in the second half of 2022.

“Data from our Phase 2 TNBC trial of trilaciclib in combination with chemotherapy showed clinically meaningful and substantial improvements in overall survival as well as enhanced measures of immune system function compared to chemotherapy alone,” said Raj Malik, M.D., Chief Medical Officer at G1 Therapeutics. “Those preliminary data support the important role trilaciclib may play in treating cancer by enhancing T cell activation and favorably altering the tumor microenvironment. This Phase 2 clinical study will support trilaciclib’s mechanistic effects potentially responsible for enhanced anti-tumor immune responses in patients and generate important data that will help guide our future development decisions across additional tumor types and new treatment combinations.”

Patient recruitment in this trial is now underway. Approximately 30 patients will be enrolled in this Phase 2 multicenter, open-label, single-arm, neoadjuvant study. Up to three tumor tissue samples will be collected for assessment. Tumor tissue will be obtained at baseline prior to study drug administration. Patients will receive a single dose of monotherapy trilaciclib, followed by a tumor biopsy approximately one week later. Following the biopsy, patients will enter the treatment phase in which trilaciclib will be administered on Day 1 of each cycle of anthracycline/cyclophosphamide for four cycles followed by trilaciclib administered on Day 1 of each weekly cycle of taxane chemotherapy for 12 cycles. Immune checkpoint inhibitor and/or carboplatin may be added to therapy at the discretion of the investigator. Three to five weeks after the last dose of chemotherapy, patients will proceed to surgery at which time a third tumor tissue sample will be collected if the patient has residual disease.

Study treatment will continue as per protocol to completion or early discontinuation of chemotherapy, until unacceptable toxicity, Investigator’s decision to withdraw the patient from study treatment, consent withdrawal, or the end of the study, whichever occurs first.

The primary objective is to evaluate the immune-based mechanism of action of trilaciclib after a single-dose as measured by the change in the ratio of CD8+ tumor-infiltrating lymphocytes (TILs) to regulatory T cell (Tregs) in the tumor microenvironment. Key secondary and exploratory endpoints include:

- Assessment of pathologic complete response (pCR) rate at the time of definitive surgery.
- Evaluation of the safety and tolerability of trilaciclib in combination with standard neoadjuvant systemic therapies.
- Tumor mRNA analyses and immunohistochemistry and peripheral blood immune profiling following trilaciclib.
- Identification of molecular and cellular biomarkers in tumor or blood samples that may be indicative of clinical response/resistance, pharmacodynamic activity, and/or the mechanism of action of trilaciclib and other systemic treatments.

About Triple Negative Breast Cancer (TNBC)
According to the American Cancer Society, nearly 300,000 new cases of invasive breast cancer are diagnosed annually in the U.S. Triple-negative breast cancer makes up approximately 15-20% of such diagnosed breast cancers. TNBC is cancer that tests negative for estrogen receptors, progesterone receptors, and excess HER2 protein. Because mTNBC cells lack key growth-signaling receptors, patients do not respond well to medications that block estrogen, progesterone, or HER2 receptors. Instead, treating mTNBC typically involves chemotherapy, radiation, and surgery. TNBC is considered to be more aggressive and have a poorer prognosis than other types of breast cancer. In general, survival rates tend to be lower with mTNBC compared to other forms of breast cancer, and mTNBC is also more likely than some other types of breast cancer to return after it has been treated, especially in the first few years after treatment. It also tends to be higher grade than other types of breast cancer.

About G1 Therapeutics
G1 Therapeutics, Inc. is a commercial-stage biopharmaceutical company focused on the development and commercialization of next generation therapies that improve the lives of those affected by cancer, including the Company’s first commercial product, COSELA™ (trilaciclib). G1 has a deep clinical pipeline and is executing a tumor-agnostic development plan evaluating trilaciclib in a variety of solid tumors, including colorectal, breast, lung, and bladder cancers. G1 Therapeutics is based in Research Triangle Park, N.C. For additional information, please visit www.g1therapeutics.com and follow us on Twitter @G1Therapeutics.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "plan," "anticipate," "estimate," "intend" and similar expressions (as well as other words or expressions referencing future

events, conditions or circumstances) are intended to identify forward-looking statements. Forward-looking statements in this press release include, but are not limited to, trilaciclib's possibility to treat cancer by enhancing T cell activation and altering the tumor microenvironment, the stated primary and secondary endpoints may not achieve statistical significance, delays in the enrollment of patients in this trial of COSELA may delay or prevent our plans, and are based on the company's expectations and assumptions as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties. Factors that may cause the company's actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in the company's filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" sections contained therein and include, but are not limited to, the company's dependence on the commercial success of COSELA; the development and commercialization of new drug products is highly competitive; the company's ability to complete clinical trials for, obtain approvals for and commercialize any of its product candidates; the company's initial success in ongoing clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials; the inherent uncertainties associated with developing new products or technologies and operating as a development-stage company; and market conditions. Except as required by law, the company assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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