G1 Therapeutics Announces Initiation of Phase 3 Registrational Study of COSELA™ (trilaciclib) in Triple-Negative Breast Cancer (TNBC)

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- PRESERVE 2 Will Evaluate Survival Benefit of COSELA in 250 Patients with Locally Advanced Unresectable or Metastatic TNBC -

RESEARCH TRIANGLE PARK, N.C., April 28, 2021 (GLOBE NEWSWIRE) -- G1 Therapeutics, Inc. (Nasdaq: GTHX), a commercial-stage oncology company, today announced the initiation of PRESERVE 2, a pivotal Phase 3, randomized, double-blind, placebo-controlled study of COSELA™ (trilaciclib) in patients receiving first- or second-line gemcitabine and carboplatin chemotherapy for locally advanced unresectable or metastatic triple-negative breast cancer (mTNBC). COSELA shows preclinical and clinical evidence of immune system enhancement which G1 is exploring in clinical trials in a variety of different tumor types to evaluate the potential of increased anti-tumor efficacy. Results of this study are expected in the second half of 2023.

“As a physician who treats people living with breast cancer, I can attest to the great need for new therapies to extend life while not adding to the side effect burden of chemotherapy,” said Joyce O'Shaughnessy, MD, Chair of Breast Cancer Research at Baylor University Medical Center, Texas Oncology, US Oncology in Dallas, TX. “Gemcitabine/carboplatin has historically been one of the standard first-line regimens for patients undergoing chemotherapy for mTNBC. In a Phase 2 study, when trilaciclib was administered prior to this regimen, it enhanced antitumor efficacy compared to gemcitabine/carboplatin alone, and improved overall survival with statistical significance. This is an important finding for patients with mTNBC, and for physicians who treat them. I’m excited to begin enrolling patients in this registrational trial and look forward to the possibility of a new, well-tolerated, and life-extending agent for my patients.”

Patient enrollment in PRESERVE 2 is now underway. The study will enroll two cohorts of patients. Cohort 1 (n=170) will evaluate patients receiving first-line therapy, regardless of PD-L1 status, who are PD-1/PD-L1 inhibitor-naïve. Cohort 2 (n=80) will evaluate PD-L1 positive patients receiving second-line therapy following prior PD-1/PD-L1 inhibitor therapy in the locally advanced unresectable/metastatic setting. These two cohorts are adequately powered and considered independent of each other. Therefore, the efficacy and safety data collected for each cohort will be analyzed separately.

Within each cohort, patients meeting entry criteria will be randomly assigned (1:1) to receive either COSELA prior to gemcitabine and carboplatin (GC) therapy (the same dosing regimen used in Group 2 of our Phase 2 study) or placebo prior to GC therapy. Study drugs will be administered intravenously (IV) on Days 1 and 8 in 21-day cycles. Study drug administration will continue until progressive disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 or clinical progression as determined by the Investigator, unacceptable toxicity, withdrawal of consent, Investigator decision, or the end of the study, whichever occurs first.

The primary endpoint in Cohort 1 is to evaluate the effect of COSELA on overall survival (OS) compared with placebo in patients receiving first-line GC. The primary endpoint of Cohort 2 is to evaluate the effect of COSELA on OS compared with placebo in patients receiving GC as second line therapy after treatment with a PD-1/PD-L1 inhibitor. Key secondary endpoints in both trials include assessment of the effect of COSELA on patients’ quality of life compared with placebo.

“Given that triple-negative breast cancer tends to be more aggressive and have a worse prognosis than other types of breast cancer, we recognize and share the urgency to conduct this trial and are enthusiastic about the potential for COSELA to significantly improve TNBC patient outcomes,” said Raj Malik, M.D., Chief Medical Officer at G1 Therapeutics. “This registrational trial follows the final data from our Phase 2 trial in mTNBC which were presented in December at the 2020 San Antonio Breast Cancer Symposium (SABCS) meeting, showing a strong survival benefit in patients receiving COSELA compared to placebo when given prior to chemotherapy, and regardless of tumor PD-L1 status. Based on those data, we believe that the unique mechanism of action of COSELA has the potential to increase antitumor efficacy and be highly beneficial to people fighting TNBC.”

Results from Randomized Phase 2 Trial of COSELA in mTNBC

New data presented at the 2020 SABCS meeting showed that COSELA significantly improved overall survival (OS) in patients with mTNBC treated with COSELA prior to administration of a chemotherapy regimen of gemcitabine/carboplatin (GC) compared with GC alone, and that COSELA enhanced immune system function. Patients were randomized to receive GC only (Group 1) or GC plus one of two dosing schedules of COSELA: COSELA administered on the day of chemotherapy (Group 2) or COSELA administered the day prior to and the day of chemotherapy (Group 3). Compared to GC alone (Group 1), statistically significant improvements in OS were achieved in both COSELA arms (Group 2: HR=0.31, p=0.0016; Group 3: HR=0.40, p=0.0004). As of the data cutoff of July 17, 2020, the median OS was 12.6 months in patients receiving GC alone, not yet reached for Group 2, and 17.8 months in Group 3. The median OS for Groups 2 and 3 combined was 19.8 months (HR=0.37, p<0.0001). Patients with both PD-L1-positive and PD-L1-negative tumors treated with COSELA and GC demonstrated improvement in OS compared to patients receiving GC alone, with the PD-L1-positive subset achieving statistically significant improvement. Data from T-cell clonality analysis suggest that administering COSELA prior to chemotherapy enhanced immune system function. (Poster here)

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 COSELA 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, COSELA's (trilaciclib) possibility to improve patient outcomes, our pivotal Phase 3 trial of COSELA in mTNBC may not be able to replicate the strong survival benefit we observed in our Phase 2 trial of COSELA in mTNBC, delays in the enrollment of patients in our Phase 3 trial of COSELA in mTNBC, may delay or prevent our plans, and COSELA may fail to achieve the degree of market acceptance for commercial success, 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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