G1 Therapeutics Presents Final Phase 2 Clinical Data on Trilaciclib in Combination with Chemotherapy in Metastatic Triple-Negative Breast Cancer Demonstrating Significant Improvement in Overall Survival at 2020 San Antonio Breast Cancer Symposium

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Company also presents updated monotherapy data on investigational oral selective estrogen receptor degrader (SERD) rintodestrant for ER+, HER2- breast cancer

RESEARCH TRIANGLE PARK, N.C., Dec. 09, 2020 (GLOBE NEWSWIRE) -- G1 Therapeutics, Inc. (Nasdaq: GTHX), a clinical-stage oncology company, today reported final data from its randomized Phase 2 trial of trilaciclib in metastatic triple-negative breast cancer (mTNBC) showing that trilaciclib significantly improved overall survival (OS) for patients treated with trilaciclib in combination with a chemotherapy regimen of gemcitabine/carboplatin (GC) compared with GC alone. These data were presented in a Spotlight Poster Discussion Session at the 2020 San Antonio Breast Cancer Symposium (SABCS). Trilaciclib is a first-in-class investigational therapy designed to improve outcomes for people with cancer treated with chemotherapy.

“Triple-negative breast cancer is the most aggressive form of breast cancer, and there is a significant need for combination therapies that extend survival for women with either PD-L1 positive or PD-L1 negative tumors,” said Raj Malik, M.D, Chief Medical Officer and Senior Vice President, R&D. “Mature data from this Phase 2 trial showed trilaciclib improved overall survival in metastatic triple-negative breast cancer when given in combination with chemotherapy, regardless of PD-L1 status. We are excited to initiate a pivotal trial of trilaciclib in mTNBC in early 2021, with the goal of confirming the promising findings from this first trial.”

Trilaciclib in combination with chemotherapy improves overall survival in mTNBC
The randomized, open-label Phase 2 trial of trilaciclib in combination with a chemotherapy regimen of GC, a current standard of care for mTNBC, enrolled 102 patients who had received up to two prior chemotherapy regimens for locally recurrent or mTNBC. In this three-arm trial, all three groups received a chemotherapy regimen of GC. Patients were randomized to receive GC only (Group 1) or GC plus one of two dosing schedules of trilaciclib: trilaciclib administered on the day of chemotherapy (Group 2) or trilaciclib administered the day prior to and the day of chemotherapy (Group 3). Preliminary data were previously reported at the 2019 European Society for Medical Oncology congress and featured in a concurrent publication in *The Lancet Oncology* (press release here).

Key findings presented in the 2020 SABCS poster included:

- Compared to GC alone (Group 1), OS was improved in both trilaciclib arms (Groups 2 and 3) (Group 2: HR=0.31, p=0.0016; Group 3: HR=0.40, p=0.0004). Median OS was 12.6 months in Group 1, not 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). OS findings in patients receiving trilaciclib were consistent with previously-reported data from this trial. The median OS for GC alone (Group 1, 12.6 months) was consistent with the previous trial findings and historical data.
- In a subset analysis based on PD-L1 status, patients with both PD-L1-positive and PD-L1-negative tumors treated with trilaciclib and GC demonstrated improvement in OS compared to patients receiving GC alone, with the PD-L1-positive subset achieving statistically significant improvement.
- In a subset analysis based on CDK4/6 status, OS was similar in tumors categorized as CDK4/6 dependent, independent, or indeterminate. In this analysis, trilaciclib did not impair the efficacy of GC, regardless of CDK4/6 status.
- Data from T-cell clonality analysis suggest that administering trilaciclib prior to chemotherapy enhanced immune system function.

Registrational trial in mTNBC to begin in 2021
This randomized, double-blind trial will evaluate trilaciclib in combination with a chemotherapy regimen of GC in two separate patient cohorts: 1) first-line treatment in patients with mTNBC who have not received a PD-1/PD-L1 inhibitor; and 2) second-line treatment in patients with mTNBC who have received a PD-1/PD-L1 inhibitor. All patients will receive treatment until disease progression. The company expects to enroll a total of approximately 250 participants in the trial, with the majority (approximately 170) in the first-line cohort. The trial will enroll patients who are both PD-L1-positive and PD-L1-negative.

The primary endpoint of this trial is overall survival; secondary endpoints include patient-reported outcomes measures, safety/tolerability, myelopreservation measures, and progression-free survival. The pre-specified statistical plan for the trial will allow for separate analysis of the two cohorts.

Updated results from rintodestrant monotherapy for ER+, HER2- breast cancer
The company also presented updated monotherapy data from the Phase 1 portion of its ongoing clinical trial of rintodestrant, a potential best-in-class oral selective estrogen receptor degrader (SERD) in development for the treatment of ER+, HER2- breast cancer. The findings included data from the 600 mg and 1,000 mg dose expansion cohorts of the trial that supported the company’s decision to advance the 800 mg dose in further development, including the ongoing rintodestrant/palbociclib arm of this trial.

Key clinical findings from the 67-patient trial (poster) included:

- Safety and tolerability findings across all doses, including the 600 mg and 1,000 mg expansion cohorts, were consistent

with previously reported data.
- In a heavily pre-treated patient population, rintodestrant showed evidence of clinical activity, including 5% (3/67) of patients with confirmed partial responses, 36% (24/67) with stable disease, and a clinical benefit rate of 30% (20/67).

About G1 Therapeutics
G1 Therapeutics, Inc. is a clinical-stage biopharmaceutical company focused on the discovery, development and delivery of next generation therapies that improve the lives of those affected by cancer. The company is developing and advancing two novel therapies. Trilaciclib is a first-in-class therapy designed to improve outcomes for patients being treated with chemotherapy. Trilaciclib received Breakthrough Therapy Designation and is under review by the U.S. Food and Drug Administration (FDA) with a PDUFA action date of February 15, 2021. Rintodestrant is a potential best-in-class oral selective estrogen receptor degrader (SERD) for the treatment of ER+ breast cancer. In 2020, the company out-licensed global development and commercialization rights to its differentiated oral CDK4/6 inhibitor, lerociclib.

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, those relating to the therapeutic potential of trilaciclib, rintodestrant and lerociclib, the timing of marketing applications in the U.S. and Europe for trilaciclib in SCLC, trilaciclib's possibility to improve patient outcomes across multiple indications, including in metastatic triple-negative breast cancer, rintodestrant's potential to be best-in-class oral SERD for treatment of ER+, HER2- breast cancer, our reliance on partners to develop and commercial licensed products, and the impact of pandemics such as COVID-19 (coronavirus), 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 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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