G1 Therapeutics Presents Phase 1 Data at ASCO Describing Favorable Safety Profile and Evidence of Antitumor Activity of Rintodestrant Combined with Palbociclib in Patients with ER+/HER2- Advanced Breast Cancer

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- Combination of Rintodestrant and Palbociclib was Very Well Tolerated with No Reported Discontinuations due to Treatment-Emergent Adverse Events (TEAEs) -

- 60% Clinical Benefit Rate Achieved in Full Analysis Set at Week 24 -

RESEARCH TRIANGLE PARK, N.C., June 04, 2021 (GLOBE NEWSWIRE) -- G1 Therapeutics, Inc. (Nasdaq: GTHX), a commercial-stage oncology company, today presented results from its Phase 1 study of its oral selective estrogen receptor degrader (SERD), rintodestrant, demonstrating the drug was very well tolerated and did not result in additional or more severe toxicities when added to palbociclib for the treatment of ER+/HER2- advanced breast cancer. In addition, encouraging antitumor activity was observed in the study, with a doubling of the clinical benefit rate (defined by percentage of patients with either confirmed complete or partial response or stable disease lasting ≥ 24 weeks) from 30 percent with rintodestrant monotherapy to 60 percent with the combination of rintodestrant and palbociclib. This effect included patients with tumors harboring ESR1 variants, which are known to modulate breast cancer severity and resistance to hormone therapy. These data are being presented at the American Society of Clinical Oncology (ASCO) annual virtual meeting, and the posters are available in the scientific publications section of G1's website.

"Between 30% and 50% of estrogen-positive tumors become resistant to selective estrogen receptor modulators (SERMs), so it is imperative that new and well tolerated approaches to overcoming resistance and improving response rates are developed," said Raj Malik, M.D., Chief Medical Officer at G1 Therapeutics. "We previously demonstrated that rintodestrant monotherapy has a favorable safety profile in patients with heavily pretreated ER+/HER2- advanced breast cancer, and the third arm now shows that the combination of rintodestrant and palbociclib provides the same favorable safety profile as well as important indicators of antitumor activity warranting further evaluation of the potential of this combination. Importantly, no ocular toxicity or bradycardia was observed during this trial, both of which are common adverse events observed in trials of other oral SERDs. These data add to the potential for rintodestrant to be an active and well-tolerated oral SERD for the treatment of ER+, HER2- breast cancer as we ultimately seek to out-license the drug."

The Phase 1, first-in-human, open-label study evaluated rintodestrant in women with ER+/HER2- advanced breast cancer after progression on endocrine therapy. The study comprised three parts: dose escalation of monotherapy rintodestrant (part 1), dose expansion of monotherapy rintodestrant (part 2), and rintodestrant in combination with palbociclib therapy (part 3). The results of part 1 and 2 were presented at the 2020 San Antonio Breast Cancer Symposium (SABCS) (2020 poster). Forty participants in the third part of the study received 800 mg of continuous rintodestrant once daily combined with 125 mg of palbociclib once daily for 21 days in 28-day cycles. This patient population had received a high degree of prior chemotherapy in the advanced setting (48%) and had visceral disease (68%); these tend to be patients that respond less well to CDK4/6 inhibitors in combination with endocrine therapies (ETs). The primary objective was safety and tolerability of rintodestrant with palbociclib, and the secondary objective was antitumor activity, including best overall response, progression-free survival (PFS), overall survival and clinical benefit rate, among other parameters.

Key study findings with a median duration of treatment of 6.2 months in the ongoing Phase 1 combination trial presented in the poster include:

Safety:

- Rintodestrant combined with palbociclib was very well tolerated, with no rintodestrant-related serious adverse events (SAEs) or dose-reductions reported.
- The addition of rintodestrant to palbociclib did not result in additional or more severe toxicities, in particular, nausea, vomiting, or diarrhea.
- The most common treatment-emergent adverse events (TEAEs) of neutropenia and leukopenia are consistent with the known safety profile of palbociclib, as previously reported.
- No discontinuations or deaths due to TEAEs were reported.
- One case (3%) each of diarrhea and fatigue was reported, but neither was considered related to the rintodestrant/palbociclib.

Antitumor Activity:

- The clinical benefit rate (CBR) doubled from 30% to 60% when palbociclib was added to rintodestrant, suggesting the potential for favorable antitumor activity in patients with ER+/HER2- advanced breast cancer, including in patients with tumors harboring ESR1 variants.
- The CBR among patients with early relapse (first metastatic recurrence while on adjuvant ET for at least 2 years' duration, or within 12 months of completing adjuvant ET) was 73% (8/11).

- In the full analysis set, 65% of patients experienced stable disease (SD).
- Median progression-free survival was 7.4 months (95% CI: 3.7 not reached), although the data are not yet mature as of the cutoff date (April 7, 2021).

The Company is in the process of evaluating partnering options for rintodestrant.

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, those relating to expectations for the therapeutic potential of rintodestrant, and the possibility to realize the economic impact in the US market presented in the scientific analyses described above, and rintodestrant 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 ability to complete a successful commercial launch for COSELA (trilaciclib); the company's ability to complete clinical trials for, obtain approvals for and commercialize any of its product candidates other than COSELA (trilaciclib); 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 commercial-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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