G1 Therapeutics Presents Phase 1b Data on G1T38 in Combination with Faslodex for Treatment of Breast Cancer at 2018 American Society of Clinical Oncology (ASCO) Annual Meeting

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RESEARCH TRIANGLE PARK, N.C., June 02, 2018 (GLOBE NEWSWIRE) -- G1 Therapeutics, Inc. (Nasdaq:GTHX), a clinical-stage oncology company, today announced that preliminary data from its Phase 1b/2a clinical trial of G1T38 in combination with Faslodex® (fulvestrant) showed promising safety, tolerability and efficacy when G1T38 was dosed continuously as a treatment for people with estrogen receptor-positive, HER2-negative (ER+, HER2-) breast cancer. These data were presented today in a poster session at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

G1T38 is an oral CDK4/6 inhibitor with broad therapeutic potential in many forms of cancer and may serve as backbone therapy for multiple combination regimens.

"The findings in this trial support continuous daily dosing of G1T38. Neutrophil declines are an important marker of effective CDK4/6 inhibition and tumor arrest, but excessive declines can result in severe neutropenia. All G1T38 dose levels studied in this trial showed neutrophil declines that plateaued after the fourth or fifth week of treatment. Preliminary efficacy results showed that 17 percent of participants had confirmed partial responses and the clinical benefit rate was 67 percent. Importantly, less than 30 percent of participants experienced Grade 3 neutropenia and all continued without dose modification. In addition, only two of 33 participants experienced Grade 4 neutropenia," said Raj Malik, M.D., Chief Medical Officer and Senior Vice President, R&D. "We have enrolled additional participants at the once-daily 400 mg and 500 mg dose levels and anticipate selecting the recommended Phase 2 dose in the near future. We expect to enroll 30 participants in the Phase 2 expansion by the end of 2018, with data reading out in 2019."

Trial Design
The Phase 1b/2a trial is designed to evaluate safety, tolerability, and establish a recommended Phase 2 dose and schedule for G1T38 administered continuously in combination with Faslodex as a treatment for ER+, HER2- breast cancer.

Data reported in the poster are as of May 1, 2018. Thirty-three trial participants received G1T38 doses ranging from 200-650 mg once daily (QD) and 100-200 mg twice daily (BID). Faslodex 500 mg QD was administered per standard of care.

Safety Findings

- There have been no G1T38-related serious adverse events reported in the trial, and no participants have withdrawn due to adverse events (AEs).
- There have been no Grade 3/4 AEs other than cytopenias, as described below.
- The most commonly reported G1T38-related AEs were cytopenias (Grades 1-4) and gastrointestinal (GI) events (Grade 1/2 only). When they occurred, GI events were transient, appeared early in therapy with a short duration, and if required, were managed with standard supportive therapies.
- There have been no reports of venous thromboembolism (VTE), QTc prolongation or drug-induced liver injury (DILI).

Neutrophil Findings
In this trial, participants continued dosing with Grade 3 neutropenia. Dose interruption followed by dose reduction was required if Grade 4 neutropenia occurred.

- Degree of neutropenia with G1T38 was consistent with effective CDK4/6 inhibition, with 73 percent all-grade neutropenia.
- Absolute neutrophil count (ANC) values plateaued after 4-5 weeks of treatment. The percent ANC change on day 29 ranged from -48 percent to -76 percent and was generally dose-dependent.
- Grade 3 neutropenia was observed in nine participants (27 percent). All participants who experienced Grade 3 neutropenia continued to receive G1T38 without dose modification.
- Two participants (6 percent) experienced Grade 4 neutropenia (200 mg QD and 500 mg QD). Both participants continued G1T38 therapy at a lower dose following a dose interruption.

Early Efficacy Findings
Early efficacy data are promising but immature. Of the 33 participants in the trial, 24 were response evaluable with measurable disease and had at least one on-treatment tumor assessment. Participants received a range of doses, some of which were below the anticipated recommended Phase 2 dose. Duration of therapy as of the data cut-off date was as follows: ≤3 months (n=14, 42 percent); > 3 – 6 months (n=5, 15 percent); > 6 – 12 months (n=10, 30 percent); and > 12 months (n=4, 12 percent).

- Partial response (PR) rate was 17 percent (4/24 response evaluable participants, all with confirmed responses).
- Clinical benefit rate (CBR), which includes complete response, partial response and stable disease for at least 24 weeks, was 67 percent (16/24 response evaluable participants).
- Stable disease rate was 71 percent (17/24 response evaluable participants).

The poster is available on the Publications page of the G1 website: http://www.g1therapeutics.com/pages/news/publications-2018.htm. Details on the presentation are available on the 2018 ASCO Annual Meeting website: http://abstracts.asco.org/.

About G1T38
G1T38 is a potential best-in-class oral CDK4/6 inhibitor being developed for use in combination with other targeted therapies in multiple oncology indications. Preliminary Phase 1b clinical data presented at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting, preclinical data presented at the 2016, 2017 and 2018 American Association for Cancer Research (AACR) Annual Meetings, and preclinical data published in *Molecular Cancer Therapeutics* and *Oncotarget* have demonstrated the compound's differentiation from other CDK4/6 inhibitors.

G1T38 is currently being evaluated in two Phase 1/2 clinical trials: a trial in combination with Faslodex® for people with ER+, HER2- breast cancer (NCT02983071), and a trial in combination with Tagrisso® for people with EGFR-mutant non-small cell lung cancer (NCT03455829).

About Faslodex®
Faslodex, developed and commercialized by AstraZeneca, represents a hormonal treatment approach that helps to slow tumor growth by blocking and degrading the estrogen receptor – a key driver of disease progression. Faslodex is indicated for the treatment of estrogen receptor positive, locally advanced or metastatic breast cancer in postmenopausal women not previously treated with endocrine therapy, or with disease relapse on or after adjuvant anti-estrogen therapy, or disease progression on anti-estrogen therapy.

Faslodex has also been licensed for use with CDK4/6 inhibitors, palbociclib (in the U.S., EU and several other markets) and abemaciclib (in the U.S. only) for the treatment of women with ER+, HER2- advanced breast cancer, whose cancer has progressed after endocrine therapy. In Japan, Faslodex is also approved for use in combination with any CDK4/6 inhibitor.

About G1 Therapeutics
G1 Therapeutics, Inc., is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for the treatment of cancer. Two of the company's pipeline assets, trilaciclib and G1T38, are CDK4/6 inhibitors, a validated and promising class of oncology therapeutics. Trilaciclib and G1T38 have broad therapeutic potential in many forms of cancer and may serve as backbone therapy of multiple combination regimens. Trilaciclib is a short-acting IV CDK4/6 inhibitor designed to preserve hematopoietic stem cell and immune system function (myelopreservation) during chemotherapy. G1T38 is a potential best-in-class oral CDK4/6 inhibitor for use in combination with other targeted therapies. G1 is also advancing G1T48, a potential best-in-class oral selective estrogen receptor degrader, or SERD, which is targeted for the treatment of ER+ breast cancer.

G1 is based in Research Triangle Park, NC. 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 news release include, but are not limited to, the therapeutic potential of trilaciclib, G1T38 and G1T48, and are based on G1 Therapeutics' 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 G1 Therapeutics' actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in G1 Therapeutics' filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" sections contained therein and include, but are not limited to, the inherent uncertainties associated with developing new products or technologies and operating as a development-stage company; G1 Therapeutics' ability to complete clinical trials for, obtain approvals for and commercialize any of its product candidates; G1 Therapeutics' ability to recruit and enroll patients in its studies; competition in the industry in which G1 Therapeutics operates; and market conditions. Except as required by law, G1 Therapeutics 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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