G1 Therapeutics Announces Upcoming 2023 Readouts from its Phase 2 and Pivotal Phase 3 Clinical Trials of Trilaciclib

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- Initial Results from Pivotal Phase 3 PRESERVE 1 Trial in Colorectal Cancer Expected in February 2023; Positive Results Would Initiate Regulatory Interactions for Label Expansion -

- Five Clinical Trials with Data Readouts in 2023 Will Evaluate Trilaciclib On-Target Effects of Myeloprotection and Enhanced Immune Function with Potential for Improved Efficacy Outcomes (Progression Free (PFS) and Overall Survival (OS)) -

- Trilaciclib's Potential Synergistic Effects with Chemotherapy, Antibody Drug Conjugates (ADCs), and Checkpoint Inhibitors Are Being Evaluated -

RESEARCH TRIANGLE PARK, N.C., Jan. 09, 2023 (GLOBE NEWSWIRE) -- G1 Therapeutics, Inc. (Nasdaq: GTHX), a commercial-stage oncology company, today announced the 2023 data readouts that are expected to drive its near-term and long-term indications and potential future treatment paradigms for some of the most aggressive and refractory cancers, including metastatic colorectal (mCRC), bladder or urothelial cancer (mUC), and triple negative breast cancer (TNBC).

"Cytotoxic therapy remains the backbone of treatment for many metastatic tumors, either alone or in combination with targeted therapies," said Raj Malik, M.D., G1's Chief Medical Officer. "But the high toxicity of these cytotoxic agents poses a risk of serious adverse events that can compromise patient well-being and patient outcomes. Trilaciclib represents a novel approach to protect against the side effects of cytotoxic therapy, but it also holds the potential to extend survival in certain cancer types, especially in combination with other novel anti-cancer interventions such as ADCs and checkpoint inhibitors—a benefit we are currently exploring in a variety of clinical trials with important readouts throughout 2023."

Trilaciclib, an IV-administered transient CDK4/6 inhibitor, is a first-in-class therapy designed to preserve bone marrow and immune system function during cytotoxic therapy to improve patient outcomes. Depending on the tumor type and the chemotherapy backbone, this mechanistic profile can drive patient benefits of myeloprotection and/or anti-tumor efficacy. Its mechanism of action of improving overall immune response by improving long term immune surveillance lends itself to longer term endpoints, such as progression free and overall survival.

Clinical Trial Results Expected in the First Quarter of 2023

PRESERVE 1: 1L mCRC registrational Phase 3 trial

February 2023: **Primary endpoint (myeloprotection)**. The Company expects to release initial results in February 2023 from the ongoing PRESERVE1 trial in patients with mCRC who received trilaciclib administered prior to treatment with FOLFOXIRI and bevacizumab. These data will include the primary myeloprotection endpoints of severe neutropenia during induction and duration of severe neutropenia in Cycles 1-4; the impact of trilaciclib on Grade 3 or 4 diarrhea; and initial patient reported outcome data. If positive, these data will serve as the basis for working closely with the FDA and other regulatory health authorities to extend the label to trilaciclib as a myeloprotective agent in patients with mCRC.

Compared to the extensive-stage small cell lung cancer market, the colorectal market is significantly larger with a longer duration of therapy (ES-SCLC: 3 months vs mCRC: 6-12 months) and CRC patients often have a better prognosis that facilitates the more aggressive therapeutic approach of FOLFOXIRI triplet therapy.

"Triplet therapy with FOLFOXIRI and bevacizumab is highly efficacious compared to doublet therapy, but it is also the most myelotoxic regimen with higher rates of neutropenia, febrile neutropenia, and diarrhea - which limits its use to a small population of 1L CRC patients," said Dr. Malik. "Trilaciclib may be an important addition to this regimen to enable a broader population of patients to benefit from this therapy and potentially further improve anti-tumor efficacy by allowing increased duration and exposure to chemotherapy."

Clinical Trial Results Expected in the Second Quarter of 2023

Phase 2 ADC trial in patients with refractory TNBC

Anti-tumor efficacy. Additional data from G1's ongoing trial of trilaciclib administered prior to the ADC sacituzumab govitecan-hziy in patients with unresectable locally advanced or metastatic TNBC are expected in 2Q23 and will include anti-tumor efficacy endpoints as measured by the primary endpoint of progression-free survival (PFS).

Initial results released in 4Q22 demonstrated the potential of trilaciclib to reduce adverse events associated with sacituzumab govitecan-hziy. Initial data on the first 18 patients show a clinically meaningful on-target effect of trilaciclib to reduce (>50%) the rates of multiple adverse events compared to the previously published sacituzumab govitecan-hziy single agent safety profile from the ASCENT trial, including myelosuppression (neutropenia, anemia, thrombocytopenia), and diarrhea and potentially alopecia due to the presence of CDK4/6-expressing cells in the intestinal crypt and hair follicles.

Phase 2 mechanism of action (MOA) trial in patients with neoadjuvant TNBC

Pathologic complete response (pCR) and immune enhancements in tumor microenvironment: Presentation of a more comprehensive data set from this 24 patient Phase 2 trial are expected in 2Q23 from analyses of the secondary endpoint of pathologic complete response rate at the time of definitive surgery and the safety of trilaciclib combined with neoadjuvant chemotherapy. Additional analyses will further elucidate the immune-based mechanism of action of a single dose of trilaciclib.

Initial results from the primary endpoint of immune-based MOA presented at the 2022 San Antonio Breast Cancer Symposium showed favorable alterations in the tumor microenvironment from a single dose of trilaciclib monotherapy as measured by an increase in the ratio of CD8+ T cells compared to regulatory T cells (Tregs).

Clinical Trial Results Expected in the Midyear 2023

PRESERVE 3: 1L bladder cancer (mUC) Phase 2 trial

Anti-tumor efficacy. Additional safety and efficacy data, including the primary endpoint of the anti-tumor efficacy of trilaciclib when combined with platinum-based chemotherapy and the checkpoint inhibitor avelumab maintenance therapy as measured by PFS are anticipated in mid-2023.

Initial results provided in January 2023 indicate that the confirmed objective response rate as of the cutoff date was comparable between arms. Longer-term follow-up is required to characterize additional anti-tumor endpoints including duration of confirmed objective response and PFS. Safety is reviewed by the data monitoring committee (DMC) on an ongoing basis, and it has recommended that the study continue as planned. Though early, the safety and tolerability profile of trilaciclib administered prior to chemotherapy is generally consistent with that expected in patients treated with gemcitabine plus cisplatin/carboplatin and avelumab maintenance for previously untreated advanced or metastatic urothelial carcinoma.

Clinical Trial Results Expected in the Second Half of 2023

PRESERVE 2: **1L metastatic TNBC registrational Phase 3 trial**

2H23: Overall survival. An interim overall survival (OS) analysis at 70% of events is currently anticipated in 2H23 to evaluate the effect of trilaciclib on overall survival in patients with TNBC when administered prior to treatment with gemcitabine and carboplatin (GC). If the interim OS analysis achieves the threshold of statistical significance required for the interim assessment showing that trilaciclib has superior efficacy in overall survival, the trial will terminate, and the data will be reported. In addition, we will discuss the data with regulatory health authorities regarding filing for potential approval of this indication.

This trial builds on the foundational Phase 2 data showing a statistically significant and medically important improvement in survival in the two arms that received trilaciclib prior to GC compared to an arm that received GC alone (HR: 0.31 and 0.40, respectively).

PRESERVE 1: **1L mCRC registrational Phase 3 trial**

4Q23: Anti-tumor efficacy. G1 expects to release initial PFS data from PRESERVE 1 on the combination of trilaciclib administered prior to FOLFOXIRI and bevacizumab in 4Q23.

These data from the five ongoing Phase 2 and pivotal Phase 3 trials of trilaciclib will inform the Company's strategic direction, clarify the potential synergistic potential of trilaciclib, and, if positive, serve as the basis for seeking additional indications beyond extensive-stage small cell lung cancer, starting with mCRC which could be approved in early 2024.

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 potential to protect against the side effects of cytotoxic therapies, extend survival in certain cancer types especially in combination with other novel anti-cancer interventions, and drive potential future cancer treatment paradigms 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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