UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): February 13, 2023 (February 9, 2023)

G1 THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-38096	26-3648180
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

700 Park Offices Drive Suite 200 Research Triangle Park, NC	27709
(Address of principal executive offices)	(zip code)

Registrant's telephone number, including area code: (919) 213-9835

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common stock, $0.0001 par value	**GTHX**	**The Nasdaq Stock Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging Growth Company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On February 13, 2023, G1 Therapeutics, Inc. issued a press release announcing the top line results from a pivotal Phase 3 trial of trilaciclib in patients receiving triplet therapy with FOLFOXIRI + bevacizumab for metastatic colorectal cancer (PRESERVE 1). A copy of the press release is attached hereto as Exhibit 99.1.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated February 13, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

G1 THERAPEUTICS, INC.

By: */s/ James Stillman Hanson*
James Stillman Hanson
General Counsel

Date: February 13, 2023

Exhibit 99.1

G1 Therapeutics Announces Top Line Results from Pivotal Phase 3 Trial of Trilaciclib in Patients Receiving Triplet Therapy with FOLFOXIRI + Bevacizumab for Metastatic Colorectal Cancer (CRC) (PRESERVE 1)

- PRESERVE 1 Achieved its Co-Primary Endpoints Showing Statistically Significant Reductions in Occurrence of Severe Neutropenia During Induction and Duration of Severe Neutropenia in Cycles 1 Through 4 -

- However, Early Anti-Tumor Efficacy Data Favored Placebo Arm Over the Trilaciclib Arm -

- Despite Achievement of Co-Primary Endpoints, G1 to Terminate PRESERVE 1 -

- Management to Host Webcast and Conference Call today at 8:30 AM ET -

RESEARCH TRIANGLE PARK, N.C., February 13, 2023 – G1 Therapeutics, Inc. (Nasdaq: GTHX), a commercial-stage oncology company, today announced topline results from its pivotal Phase 3 PRESERVE 1 trial showing that the trial achieved its co-primary endpoints related to severe neutropenia with statistical significance; however, early anti-tumor efficacy data, including overall response rate (ORR) and preliminary measures of survival, favored the placebo arm. Other clinical trials of trilaciclib in combination with different chemotherapies in patients with extensive-stage small cell lung cancer and triple negative breast cancer did not demonstrate this adverse survival signal. Given that placebo outperformed trilaciclib in these analyses of PRESERVE 1, the Company has made the decision to discontinue the colorectal (CRC) trial. The Data Monitoring Committee (DMC) has independently reached the same conclusion.

PRESERVE 1 was designed to evaluate the efficacy and safety of trilaciclib administered in addition to triplet therapy with FOLFOXIRI + bevacizumab in patients with metastatic CRC. Detailed Phase 3 results will be presented at an upcoming scientific congress and submitted for publication.

PRESERVE 1 achieved its co-primary endpoints showing clinically meaningful and statistically significant reductions in both occurrence of severe neutropenia during induction (placebo=20% vs. trilaciclib=1%; $p<0.001$) and mean duration of severe neutropenia in Cycles 1 through 4 (placebo=1.3 days vs. trilaciclib=0.1 days; $p<0.001$). In addition, patients receiving trilaciclib had a clinically meaningful reduction in the rate of chemotherapy-induced diarrhea, including a 50% reduction in the rate of Grade 3/4 diarrhea and a 30% reduction in the rate of any grade diarrhea, compared to placebo. Further, patients receiving trilaciclib experienced fewer chemotherapy dose reductions and delays. Other secondary measures of myeloprotection also favored trilaciclib, including reductions in Febrile Neutropenia (placebo=5% vs. trilaciclib=0%) and ESA administration (placebo=7% vs. trilaciclib=3%).

However, despite the achievement of the co-primary endpoints and other secondary measures of myeloprotection and tolerability, early anti-tumor efficacy data, including overall response rate (ORR), favor patients receiving placebo compared to trilaciclib (61% and 50% ORRs, respectively). Given the differential in these anti-tumor efficacy metrics and the low likelihood of achieving the progression-free survival (PFS) and overall survival (OS) endpoints, G1 has made the decision to discontinue PRESERVE 1.

“PRESERVE 1 is the first clinical evaluation of trilaciclib in a 5-FU-based chemotherapeutic backbone,” said Raj Malik, M.D., G1 Therapeutics’ Chief Medical Officer. “This study reaffirms that trilaciclib is a highly effective drug for myeloprotection that all but eliminated neutropenia as a concern for patients with CRC in the trial, which helps inform our ongoing combination studies with other highly myelotoxic

regimens like ADCs. Unfortunately, despite the robust myeloprotection and improved tolerability, early survival indicators, including the observed overall response rate in this trial, favor patients receiving placebo. These results in PRESERVE 1 are inconsistent with what we've observed in other tumors with different chemotherapy backbones. As a result of these topline results, we have made the decision to terminate this study. While we are disappointed, we are grateful for the patients, clinical investigators and their office staff, our partner Simcere, and the G1 team—all of whom contributed to the conduct of this trial."

"All of us at G1 are disappointed in this surprising outcome for patients with CRC, but we remain committed to the potential of trilaciclib to impact the lives of many cancer patients in other indications," said Jack Bailey, G1 Therapeutics' Chief Executive Officer. "We are increasingly encouraged by the real-world performance of trilaciclib in patients with extensive stage small cell lung cancer and look forward to upcoming readouts in our other ongoing trials."

About PRESERVE 1

PRESERVE 1 is a global multi-center, randomized placebo-controlled, line extension pivotal Phase 3 trial of trilaciclib in 326 patients with metastatic CRC receiving first line trilaciclib administered to triplet therapy with FOLFOXIRI (fluorouracil (5-FU), folinic acid, oxaliplatin and irinotecan) and bevacizumab. The regimen was given for two consecutive days of every 14-day cycle. Patients received trilaciclib or placebo administered prior to their chemotherapy for a maximum of 12 cycles of induction followed by maintenance therapy.

Webcast and Conference Call

G1 will host a webcast and conference call at 8:30 a.m. ET today to discuss PRESERVE 1 and the Company's ongoing commercial and clinical programs.

Please note that there is a new process to access the call via telephone. To register and receive a dial in number and unique PIN to access the live conference call, please follow this link to register online. While not required, it is recommended that you join 10 minutes prior to the start of the event. A live and archived webcast will be available on the Events & Presentations page of the company's website: www.g1therapeutics.com. The webcast will be archived on the same page for 90 days following the event.

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 development plan evaluating trilaciclib in a variety of solid tumors, including 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.

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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 myelotoxic cytotoxic therapies including in combination with ADCs, the success of our ongoing clinical trials, and our development plan evaluating trilaciclib in a variety of solid tumors 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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