Initial Results from Phase 2 Trial Demonstrate Potential of Trilaciclib to Reduce Adverse Events Related to an Antibody Drug Conjugate (ADC)

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- Data Suggest On-Target Effect of Trilaciclib May Reduce Rates of Myelosuppression, Diarrhea, and Potentially Alopecia Associated with Sacituzumab Govitecan-Hziy -

RESEARCH TRIANGLE PARK, N.C., Nov. 02, 2022 (GLOBE NEWSWIRE) -- G1 Therapeutics, Inc. (Nasdaq: GTHX), a commercial-stage oncology company, today described safety data from the first 18 patients enrolled in its ongoing Phase 2, single arm study of trilaciclib administered prior to the antibody-drug conjugate (ADC), sacituzumab govitecan-hziy in patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC). These initial data highlight the potential for trilaciclib to meaningfully reduce adverse events related to use of sacituzumab.

“Though the data are preliminary, we are seeing encouraging and consistent reductions in the rate of adverse events related to use of sacituzumab govitecan-hziy when trilaciclib is administered prior to the ADC, relative to the previously published single agent safety profile of this ADC, including those related to myelosuppression,” said Raj Malik, M.D., Chief Medical Officer at G1 Therapeutics. “We believe we are seeing on-target effects of trilaciclib in the expected reduction in the rate of myelosuppression and in the rates of diarrhea and potentially alopecia. We will continue to progress this trial and look forward to presenting a more comprehensive data set including initial efficacy results at a medical meeting in the second quarter of 2023.”

Preliminary Safety Data (n=18): Trilaciclib is well tolerated when administered prior to sacituzumab. 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.

Summary of treatment-emergent adverse events (TEAEs) (≥ 15% of patients) in patients receiving trilaciclib in combination with sacituzumab govitecan-hziy

Phase 2 trial of trilaciclib in combination with sacituzumab govitecan-hziy TEAEs (n=18)

Adverse Event	Any Grade	Grade 3-4
Fatigue	44%	0%
Nausea	39%	0%
Constipation	28%	0%
Diarrhea	28%	0%
Headache	28%	0%
Neutropenia	22%	17%
Decreased Appetite	22%	0%
Leukopenia	17%	17%

Summary of TEAEs in patients receiving sacituzumab govitecan-hziy[1]

(Only includes TEAEs also reported in patients receiving trilaciclib and sacituzumab govitecan-hziy)

ASCENT TEAEs (no trilaciclib) (n=258)

Adverse Event	Any Grade	Grade 3-4
Fatigue	52%	4%
Nausea	62%	<4%
Constipation	37%	<1%
Diarrhea	65%	11%
Headache	18%	1%
Neutropenia	64%	52%
Decreased Appetite	28%	2%
Leukopenia	17%	10%

[1]Adapted from Bardia A, *et al.* Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med 2021;384:1529-41. DOI: 10.1056/NEJMoa2028485. Table S1

Summary of other relevant TEAEs in patients receiving trilaciclib in combination with sacituzumab govitecan-hziy

Summary of other relevant treatment-related adverse events (TRAEs) in patients receiving sacituzumab govitecan-hziy[2]

Phase 2 trial of trilaciclib in combination with sacituzumab govitecan-hziy TEAEs (n=18)		
Adverse Event	**Any Grade**	**Grade 3-4**
Anemia	6%	0%
Febrile Neutropenia	0%	0%
Thrombocytopenia	0%	0%

ASCENT TRAEs (no trilaciclib) (n=258)		
Adverse Event	**Any Grade**	**Grade 3-4**
Anemia	34%	8%
Febrile Neutropenia	6%	6%
Thrombocytopenia	5%	2%

[2]Adapted from Bardia A, *et al.* Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med 2021;384:1529-41. DOI: 10.1056/NEJMoa2028485. Table 3

Phase 2 Trial Design

This is an exploratory Phase 2, multicenter, open-label, single arm study evaluating the safety and efficacy of trilaciclib administered prior to sacituzumab govitecan-hziy in patients with unresectable, locally advanced or metastatic TNBC who received at least 2 prior treatments, at least 1 in the metastatic setting. Trilaciclib will be administered as a 30-minute IV infusion completed within 4 hours prior to the start of sacituzumab govitecan-hziy treatment on day 1 and day 8 of each 21-day cycle.

The primary objective is to evaluate the anti-tumor efficacy of trilaciclib when administered prior to sacituzumab govitecan-hziy as measured by progression-free survival (PFS). Key secondary endpoints include evaluation of the anti-tumor efficacy as measured by the objective response rate (ORR), duration of objective response (DOR), clinical benefit rate (CBR), and overall survival (OS); and evaluation of the myeloprotective effects of trilaciclib.

About Triple Negative Breast Cancer (TNBC)

According to the American Cancer Society, nearly 300,000 new cases of invasive breast cancer are diagnosed annually in the U.S. Triple-negative breast cancer makes up approximately 15-20% of such diagnosed breast cancers. TNBC is cancer that tests negative for estrogen receptors, progesterone receptors, and excess HER2 protein. Because mTNBC cells lack key growth-signaling receptors, patients do not respond well to medications that block estrogen, progesterone, or HER2 receptors. Instead, treating mTNBC typically involves chemotherapy, radiation, and surgery. TNBC is considered to be more aggressive and have a poorer prognosis than other types of breast cancer. In general, survival rates tend to be lower with mTNBC compared to other forms of breast cancer, and mTNBC is also more likely than some other types of breast cancer to return after it has been treated, especially in the first few years after treatment. It also tends to be higher grade than other types of breast cancer.

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, trilaciclib's ability to reduce adverse events related to use of sacituzumab govitecan-hziy when administered prior to the ADC, trilaciclib's ability to act synergistically with an ADC to improve patient outcome and reduce myelosuppressive side effects (neutropenia, anemia, thrombocytopenia), and diarrhea, and potentially alopecia, and delays in the enrollment of patients in this trial of trilaciclib may delay or prevent our plans, 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 (trilaciclib); 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 commerical-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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