Meaningful Improvement in Overall Survival (OS) and Tolerability Observed in Patients Receiving Trilaciclib in Combination with a TROP2 Antibody-Drug Conjugate (ADC)

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- New Positive Phase 2 Results in Metastatic Triple Negative Breast Cancer (mTNBC) Indicate That Use of Trilaciclib in Combination with a TROP2 ADC May Be Associated with Improved Median OS Compared to Historical Data for the ADC Alone -

- Exploratory Analysis of a More Comparable Patient Population Showed an Approximately Six-Month Improvement in Median OS Among Patients Receiving Trilaciclib in Combination with the ADC Compared to Historical ADC Data -

- Prolonged OS Observed in Patients Receiving Trilaciclib with Prior Anti-PD-(L)1 Therapy and No Prior Oral CDK4/6 Inhibitor -

- On-Target Effect of Trilaciclib Reduces Rates of Multiple Adverse Events Associated with the TROP2 ADC Including Myelosuppression and Diarrhea -

- Results to be Presented at the 2024 American Society of Clinical Oncology (ASCO) Meeting -

RESEARCH TRIANGLE PARK, N.C., May 28, 2024 (GLOBE NEWSWIRE) -- G1 Therapeutics, Inc. (Nasdaq: GTHX), a commercial-stage oncology company, today announced the presentation of mature Phase 2 clinical trial results describing the positive impact of trilaciclib in combination with a TROP2 ADC (sacituzumab govitecan; SG) on overall survival (OS) and tolerability compared to SG alone based on historical data from the ASCENT trial[1]. The poster is being presented during the Breast Cancer-Metastatic poster session at the 2024 American Society of Clinical Oncology (ASCO) meeting, held May 31 to June 4, 2024, and will be made available once the poster is presented on June 2, 2024 on the G1 Therapeutics website here.

The poster entitled, "*Trilaciclib Combined with Sacituzumab Govitecan (SG) in Metastatic Triple Negative Breast Cancer (mTNBC): Updated Phase 2 Safety and Efficacy Results*" (Seneviratne, L. *et al*.) (abstract number 1091) describes the mature results from a Phase 2 trial of trilaciclib in combination with SG in patients with mTNBC. These results indicate that patients in the intent-to-treat (ITT) population receiving trilaciclib with the ADC experienced an approximately four-month improvement in median OS (15.9 months vs 12.1 months) compared to that expected from the ADC alone based on historical data from the ASCENT trial and had a 12-month survival of 60%. Further, in an exploratory analysis of a potentially more comparable patient population to that enrolled in the ASCENT trial, a 48% or approximately six-month improvement in median OS (17.9 months vs 12.1 months) was observed in patients receiving trilaciclib in combination with SG compared to historical data from SG alone. Prolonged OS was observed in patients receiving trilaciclib with the ADC who had an initial breast cancer diagnosis of TNBC, prior use of checkpoint inhibitors, and no prior oral CDK4/6 inhibitor use. The poster also describes the significant on-target benefit of trilaciclib in reducing adverse events associated with this ADC, including diarrhea, neutropenia, anemia, and thrombocytopenia. These results support further evaluation of trilaciclib prior to SG or other ADCs and will help determine the design of future pivotal combination trials.

"While the development of therapies for the HER2+ and ER+ spectrum of disease is advancing quickly, TNBC remains an area where we continuously seek to identify important therapeutic signals with improved outcomes that should be further developed in well-controlled pivotal clinical trials," said Lasika Seneviratne, M.D., Chief Medical Officer at Los Angeles Cancer Network and Chief Scientific Officer of the Research Division of the Los Angeles Cancer Network (LACN). "In this trial, trilaciclib significantly reduced the side effect burden – neutropenia and diarrhea in particular – associated with sacituzumab which can meaningfully improve the tolerability of this important therapy. And although cross-trial comparisons should be made with caution, we observed a strong survival signal associated with use of trilaciclib prior to sacituzumab in the ITT population in this trial compared to the historical expectation of the ADC alone, and an even stronger signal in the potentially more comparable data that censored patients who received subsequent therapy with an ADC that was not approved for patients with HER-2 low breast cancer at the time of ASCENT. These are important and consistent hypothesis-generating Phase 2 results that may, with further testing, provide an opportunity to change the therapeutic landscape for patients living with TNBC."

The Phase 2 multicenter, open-label, single arm trial enrolled 30 patients with unresectable, locally advanced or metastatic TNBC who received at least two prior treatments, at least one in the metastatic setting. Trilaciclib was administered as a 30-minute IV infusion completed within 4 hours prior to the start of SG treatment on day 1 and day 8 of each 21-day cycle. The primary endpoint was progression-free survival (PFS) per RECIST v1.1. Key

secondary endpoints included overall survival (OS), myeloprotection, and safety/tolerability, as well as objective response rate (ORR), clinical benefit rate (CBR; confirmed complete response, partial response, or stable disease lasting ≥ 24 weeks from first dose), and duration of response (DOR).

Patient Demographics

Enrolled patients (n=30) received a median of 6.0 cycles of treatment, and median follow-up was 15.0 months. One patient remains on study treatment and 12 patients remain in the study. The median age of patients enrolled in the trial was 56.0 years. This trial included a highly pretreated population of patients: 77% (23 of 30) received 2 or 3 prior systemic anticancer regimens, and 23% (7 of 30) received greater than 3 prior systemic anticancer regimens. A majority (73%; 22/30) of patients received prior PD-(L)1 immunotherapy compared to 29% in the ASCENT trial and 20% (6/30) of patients received prior oral CDK4/6 inhibitor treatment. Sixty-seven percent (67%; 20/30) of patients had an initial diagnosis of TNBC. Thirty percent (30%; 9/30) of patients received subsequent anticancer therapy with fam-trastuzumab deruxtecan-nxki (T-DXd).

Key Survival Analyses (n=30)

- In the overall ITT population, patients receiving trilaciclib prior to SG experienced a median OS of 15.9 months compared to the expected 12.1 months for SG alone based on historical data from the ASCENT trial. Twelve-month OS was 60%.
- Since the conclusion of the ASCENT trial, the treatment landscape has evolved and T-DXd has since been approved for use in patients with HER2-low disease. Given that it was not an approved indication for T-DXd at the time of ASCENT, an analysis was conducted to exclude patients who received subsequent anticancer therapy (SACT) with T-DXd by censoring patient data from the start of SACT with T-DXd for those patients who received it. The outcomes in this censored population are potentially more comparable to results from the ASCENT study. In this patient population, median OS among patients receiving trilaciclib was 17.9 months vs. 12.1 for SG alone.

Exploratory Survival Analyses

- All patients were diagnosed with unresectable, locally advanced or metastatic TNBC at the time of study entry. However, in patients who had an initial breast cancer diagnosis of TNBC (n=20), median OS was 17.9 months compared to 12.0 months in those without TNBC as the initial diagnosis.
- In patients who had previously received checkpoint inhibitor therapy with PD-(L)1 inhibitors (n=22), median OS was 18.1 months compared to 11.4 months in patients who did not receive checkpoint inhibitor therapy.
- In patients who did not receive prior oral CDK4/6i therapy (n=24), median OS was 17.9 months compared to 8.0 months in those who did.

In the overall population (N = 30), confirmed CBR was 47% (14/30). ORR was 23% (7/30), with median DOR of 9.1 months. Median PFS with trilaciclib administered prior to SG was 4.1 months, unchanged from the initial efficacy analysis presented at the European Society for Medical Oncology (ESMO) Breast Cancer 2023 meeting.

Safety Data (n=30)

Trilaciclib was well tolerated when administered prior to SG. Mature safety results show a clinically meaningful on-target effect of trilaciclib to reduce the rates of multiple treatment emergent adverse events (TEAEs) associated with SG compared to the previously published SG single agent safety profile from the ASCENT trial, including measures of myelosuppression (neutropenia, anemia, thrombocytopenia) and diarrhea due to the presence of CDK4/6-expressing cells in the intestinal crypt.

Summary of TEAEs in patients receiving trilaciclib in combination with SG		
Phase 2 trial of trilaciclib in combination with sacituzumab: TEAEs (n=30)		
Adverse Event	**Any Grade**	**Grade 3-4**
Diarrhea	43%	7%
Neutropenia	40%	23%
Anemia	10%	3%
Thrombocytopenia	0%	0%

Summary of TEAEs in patients receiving SG*		
ASCENT (no trilaciclib): TEAEs (n=258)		
Adverse Event	**Any Grade**	**Grade 3-4**
Diarrhea	65%	11%
Neutropenia	64%	52%
Anemia	34%	6%
Thrombocytopenia	5%	2%

*Adapted from A Bardia, *et al.*, Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer, N Engl J Med 2021; 384:1529-1541

“These mature Phase 2 results are compelling and will be essential to determining the design of future pivotal combination trials,” said Raj Malik, MD, G1 Therapeutics’ Chief Medical Officer. “In particular, the approximately six-month improvement in OS observed in the patient population that more closely mirrors that of the ASCENT trial indicates an opportunity to meaningfully enhance the therapeutic potential of a TROP2 ADC. We look forward to sharing these data with the medical community at ASCO, and to identifying the right partners to support advancement of this important combination.”

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 a 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 oncology biopharmaceutical company whose mission is to develop and deliver next-generation therapies that improve the lives of those affected by cancer, including the Company's first commercial product, COSELA® (trilaciclib). The Company is also evaluating therapies in combination with cytotoxic therapies and/or immunotherapy in areas of high unmet need including triple-negative breast cancer and extensive stage small cell lung cancer. G1's goal is to provide innovative therapeutic advances for people living with cancer. G1 is based in Research Triangle Park, N.C. For additional information, please visit http://www.g1therapeutics.com and follow us on X (formerly known as Twitter) @G1Therapeutics and LinkedIn.

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," "could", "believe," "goal", "projections," "estimate," "intend," "indicate," "potential," "promising," "opportunity," "suggest," 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, the ability of trilaciclib to significantly reduce the side effect burden associated with this sacituzumab which can meaningfully improve the tolerability of this ADC, and that these are hypothesis-generating Phase 2 results that may, with further testing, change the therapeutic landscape for these patients, 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 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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[1] Bardia *et al.* Final Results from the Randomized Phase III ASCENT Clinical Trial in Metastatic Triple-Negative Breast Cancer and Association of Outcomes by Human Epidermal Growth Factor Receptor 2 and Trophoblast Cell Surface Antigen 2 Expression." *Journal of Clinical Oncology* (2024): JCO-23.

Source: G1 Therapeutics