TG Therapeutics Announces Presentation of Data from the ULTIMATE I & II Phase 3 Trials of Ublituximab in Multiple Sclerosis at 7th Congress of the European Academy of Neurology

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NEW YORK, June 18, 2021 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced the presentation of data from the ULTIMATE I & II global, active controlled, Phase 3 trials evaluating ublituximab, the Company's investigational novel, glycoengineered anti-CD20 monoclonal antibody, compared to teriflunomide, in patients with relapsing forms of multiple sclerosis (RMS), during the 7th Congress of the European Academy of Neurology (EAN). This data was previously presented at the American Academy of Neurology (AAN) 73rd Annual Meeting.

Oral Presentation Title: Ublituximab versus teriflunomide in relapsing multiple sclerosis (RMS): Results of the Phase 3 ULTIMATE I and II trials

The ULTIMATE I & II studies investigated the safety and efficacy of a one-hour 450mg infusion of ublituximab every six months, following the Day 1 infusion (150mg over four hours). The studies were conducted under Special Protocol Assessment (SPA) agreement with the U.S. Food and Drug Administration (FDA). Additionally, data from these studies are intended to support a Biologics License Application (BLA) submission for ublituximab in RMS targeted in the third quarter of 2021.

Data highlights from the ULTIMATE I & II Phase 3 studies in patients with RMS include:

Primary Endpoint: Annualized Relapse Rate (ARR) Results

- In ULTIMATE I, treatment with ublituximab resulted in an ARR of 0.076 compared to 0.188 for teriflunomide, representing a relative reduction of approximately 60% (p<0.0001).
- In ULTIMATE II, treatment with ublituximab resulted in an ARR of 0.091 compared to 0.178 for teriflunomide, representing a relative reduction of approximately 50% (p=0.0022).

MRI Results

- Total number of T1 Gadolinium (Gd) enhancing lesions were reduced as a result of ublituximab treatment by 97% and 96% relative to treatment with teriflunomide in ULTIMATE I & II, respectively (p<0.0001).
- New or enlarging T2 lesions were reduced as a result of ublituximab treatment by 92% and 90% relative to treatment with teriflunomide in ULTIMATE I & II, respectively (p<0.0001).

No Evidence of Disease Activity (NEDA) Results

- In ULTIMATE I, 44.6% of ublituximab treated patients achieved NEDA representing a 198% improvement over teriflunomide (p <0.0001).
- In ULTIMATE II, 43% of ublituximab treated patients achieved NEDA representing a 277% improvement over teriflunomide (p<0.0001).

Prespecified Pooled Disability Results

- A very low rate of disability progression was observed across all treatment groups. Only 5.2% of ublituximab treated patients showed a 12-week Confirmed Disability Progression (CDP), compared to 5.9% with teriflunomide, and only 3.3% of ublituximab treated patients showeda 24-week CDP, compared to 4.8% with teriflunomide; neither was statistically different.
- Ublituximab treatment increased the proportion of patients with 12-week Confirmed Disability Improvement (CDI) and 24-week CDI, demonstrating a 116% increased chance in 12-week CDI (12% v. 6%; p=0.0003), and a 103% increased chance in 24-week CDI (9.6% v. 5.1%; p=0.0026) compared to teriflunomide.

Ublituximab was generally well tolerated with no unexpected safety signals. Overall, the proportion of patients in the ublituximab group with adverse events was similar to the teriflunomide group in a pooled analysis of both studies (approximately 88% in each treatment group); the most common adverse event associated with ublituximab was infusion related reactions (47.7% of patients who received ublituximab experienced at least one infusion-related reaction vs. 12.2 percent for the teriflunomide group).

ABOUT THE ULTIMATE I & II TRIALS
ULTIMATE I and ULTIMATE II are two independent Phase 3, randomized, double-blinded, active-controlled, global, multi-center studies evaluating the efficacy and safety/tolerability of ublituximab (450mg dose administered by one-hour intravenous infusion every 6 months, following a Day 1 infusion of 150mg over four hours and a Day 15 infusion of 450mg over one hour) versus teriflunomide (14mg oral tablets taken once daily) in subjects with relapsing forms of Multiple Sclerosis (RMS). The ULTIMATE I & II trials enrolled a total of 1,094 patients with RMS across 10 countries. These trials were led by Lawrence Steinman, MD, Zimmermann Professor of Neurology & Neurological Sciences, and Pediatrics at Stanford University and were

conducted under a Special Protocol Assessment (SPA) agreement with the U.S. Food and Drug Administration (FDA). Both studies have met their primary endpoint with ublituximab treatment demonstrating a statistically significant reduction in annualized relapse rate (ARR) over a 96-week period ($p<0.005$ in each trial). Ublituximab treatment resulted in an ARR of <0.10 in each of ULTIMATE I & II, with a relative reduction in ARR of approximately 60% and 50%, respectively, over teriflunomide. Key secondary MRI endpoints have also been met. Data from these studies are intended to support a Biologics License Application (BLA) submission for ublituximab in RMS targeted Q3 2021. Additional information on these clinical trials can be found at www.clinicaltrials.gov (NCT03277261; NCT03277248).

ABOUT UBLITUXIMAB
Ublituximab is an investigational glycoengineered monoclonal antibody that targets a unique epitope on CD20-expressing B-cells. When ublituximab binds to the B-cell it triggers a series of immunological reactions, including antibody-dependent cellular cytotoxicity (ADCC) and complement dependent cytotoxicity (CDC), leading to destruction of the cell. Additionally, ublituximab is uniquely designed, to lack certain sugar molecules normally expressed on the antibody. Removal of these sugar molecules, a process called glycoengineering, has been shown to enhance the potency of ublituximab, especially the ADCC activity. Targeting CD20 using monoclonal antibodies has proven to be an important therapeutic approach for the management of B-cell malignancies and autoimmune disorders, both diseases driven by the abnormal growth or function of B-cells.

ABOUT MULTIPLE SCLEROSIS
Relapsing multiple sclerosis (RMS) is a chronic demyelinating disease of the central nervous system (CNS) and includes people with relapsing-remitting multiple sclerosis (RRMS) and people with secondary progressive multiple sclerosis (SPMS) who continue to experience relapses. RRMS is the most common form of multiple sclerosis (MS) and is characterized by episodes of new or worsening signs or symptoms (relapses) followed by periods of recovery. It is estimated that nearly 1 million people are living with MS in the United States and approximately 85% are initially diagnosed with RRMS.[1,2] The majority of people who are diagnosed with RRMS will eventually transition to SPMS, in which they experience steadily worsening disability over time. Worldwide, more than 2.3 million people have a diagnosis of MS.[1]

ABOUT TG THERAPEUTICS, INC.
TG Therapeutics is a fully-integrated, commercial stage biopharmaceutical company focused on the acquisition, development and commercialization of novel treatments for B-cell malignancies and autoimmune diseases. In addition to an active research pipeline including five investigational medicines across these therapeutic areas, TG has received accelerated approval from the U.S. FDA for UKONIQ® (umbralisib), for the treatment of adult patients with relapsed/refractory marginal zone lymphoma who have received at least one prior anti-CD20-based regimen and relapsed/refractory follicular lymphoma who have received at least three prior lines of systemic therapies. Currently, the Company has two programs in Phase 3 development for the treatment of patients with relapsing forms of multiple sclerosis (RMS) and patients with chronic lymphocytic leukemia (CLL) and several investigational medicines in Phase 1 clinical development. For more information, visit www.tgtherapeutics.com, and follow us on Twitter @TGTherapeutics and Linkedin.

UKONIQ® is a trademark of TG Therapeutics, Inc.

Cautionary Statement
This press release contains forward-looking statements that involve a number of risks and uncertainties. For those statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. Such forward looking statements include but are not limited to statements regarding the results of the ULTIMATE I & II studies and the Company's plans and timelines for submission of a Biologics License Application (BLA) for ublituximab for the treatment of relapsing forms of Multiple Sclerosis (RMS).

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release. In addition to the risk factors identified from time to time in our reports filed with the U.S. Securities and Exchange Commission (SEC), factors that could cause our actual results to differ materially include the following: the risk that the data from the ULTIMATE I & II trials that we announce or publish may change, or the perceived product profile may be impacted, as more data or additional endpoints (including efficacy and safety) are analyzed; the risk that safety issues will emerge despite our belief that there were no unexpected safety signals identified in the ULTIMATE I & II trials ; our ability to complete the BLA submission for ublituximab in RMS within the timeline projected and the risk that FDA will not accept the submission; the risk that the clinical results from the ULTIMATE I & II trials will not support regulatory approval of ublituximab to treat RMS for efficacy, safety or other issues or, if approved, that we will not receive regulatory approval within the timeline projected; the risk that if approved, ublituximab will not be commercially successful; our ability to expand our commercial infrastructure, and successfully launch, market and sell ublituximab in RMS if approved; the Company's reliance on third parties for manufacturing, distribution and supply, and a range of other support functions for our commercial and clinical products, including ublituximab; the uncertainties inherent in research and development; and the risk that the ongoing COVID-19 pandemic and associated government control measures have an adverse impact on our research and development plans or commercialization efforts. Further discussion about these and other risks and uncertainties can be found in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and in our other filings with the SEC. Any forward-looking statements set forth in this press release speak only as of the date of this press release. We do not undertake to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof. This press release and prior releases are available at www.tgtherapeutics.com. The information found on our website is not incorporated by reference into this press release and is included for reference purposes only.

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1. MS Prevalence. National Multiple Sclerosis Society website. https://www.nationalmssociety.org/About-the-Society/MS-Prevalence. Accessed October 26, 2020. **2.** Multiple Sclerosis International Federation, 2013 via Datamonitor p. 236.