TG Therapeutics Announces Data Presentations from the ULTIMATE I & II Phase 3 Trials of Ublituximab in Multiple Sclerosis Presented at the Americas Committee for Treatment and Research in Multiple Sclerosis Annual Forum

February 25, 2022

NEW YORK, Feb. 25, 2022 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced data presentations at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) annual forum, including additional analyses from the ULTIMATE I & II 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). Highlights from the data presentations are included below.

Michael S. Weiss, Chairman and Chief Executive Officer of TG Therapeutics stated, "We are excited to share three new data presentations from the ULTIMATE I & II Phase 3 trials at the ACTRIMS annual forum. The data presented yesterday continue to highlight the benefits of ublituximab as a potential treatment option for patients with RMS. We look forward to continuing to evaluate data from the ULTIMATE I & II Phase 3 trials as we head toward our FDA PDUFA goal date of September 28, 2022 for ublituximab in RMS."

Poster Presentation Title: Reduction in T1 Hypointense Lesions With Ublituximab vs Teriflunomide in the Phase 3 ULTIMATE I and II Studies in Relapsing Multiple Sclerosis

- In pooled post hoc analyses, significant reductions in both the volume and number of new T1 hypointense lesions were seen with ublituximab vs teriflunomide at 96 weeks
  - Mean change from baseline at 96 weeks (across all postbaseline timepoints) in T1 hypointense lesion volume was 4.9x lower ublituximab compared to teriflunomide, 0.0101 vs. 0.0491 respectively, a difference of -0.0390 (95% confidence interval, -0.0585 to -0.0195; P<0.0001)
  - Mean number ± standard deviation of new T1 hypointense lesions at 96 weeks was significantly reduced (3.6x reduction) with ublituximab vs teriflunomide (1.5±3.55 vs 5.4±10.67, respectively; P<0.0001)

Poster Presentation Title: Neutralizing Antibodies and Antidrug Antibodies in the Ublituximab Phase 3 ULTIMATE I and II Studies in Relapsing Multiple Sclerosis

- In the Phase 3 ublituximab studies:
  - The proportion of patients receiving ublituximab who tested positive for Nabs and ADAs was 2.4% and 17.8% at baseline and 6.4% and 86.5% at any time postbaseline, respectively, however this reduced to 1.1% and 16.5% at Week 96, and were not found to impact efficacy as measured by annualized relapse rate (ARR) or the number of new/enlarging T2 lesion
  - The proportion of patients with TE-NAbs and TE-ADAs declined after 24 weeks, with continued reductions at subsequent timepoints
  - TE-ADAs were generally transient and had no observable impact on B-cell depletion or ublituximab's efficacy or tolerability

Poster Presentation Title: Pharmacodynamics of B-Cell Depletion and Pharmacokinetics of the Novel Anti-CD20 Monoclonal Antibody Ublituximab in Patients With Relapsing Multiple Sclerosis

- In ULTIMATE I and II, peripheral B-cell numbers declined rapidly after the first ublituximab infusion and remained low during treatment, which is consistent with ublituximab's mechanism of action
  - Starting at Week 1 Day 2, patients had a notable decrease from baseline in the mean number of CD19+ B cells (96.2% reduction), which remained consistent through Week 96 (97.6% reduction)
  - Prior to the first open-label extension (OLE) infusion, an average of 55 weeks after the last infusion, mean B-cell numbers had increased to 23.8% of baseline

Copies of the above presentations are available on the Publications page, located within the Pipeline section, of the Company's website at www.tgtherapeutics.com/publications.cfm.

ABOUT THE ULTIMATE I & II PHASE 3 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). As previously announced, both

studies met their primary endpoint with ublituximab treatment demonstrating a statistically significant reduction in annualized relapse rate (ARR) compared to terifunomide over a 96-week period (p<0.005 in each trial). 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 three 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 registered 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 ublituximab as a potential treatment for relapsing forms of Multiple Sclerosis (RMS), the results of the ULTIMATE I & II Phase 3 studies, and the timing of FDA review of the Biologics License Application for ublituximab in 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 are analyzed; the risk that data may emerge from future clinical studies or from adverse event reporting that may affect the perceived safety and tolerability profile and commercial potential of ublituximab; 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.

CONTACT:

Investor Relations
Email: ir@tgtxinc.com
Telephone: 1.877.575.TGTX (8489), Option 4

Media Relations:
Email: media@tgtxinc.com
Telephone: 1.877.575.TGTX (8489), Option 6

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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.