TG Therapeutics Announces Data Presentations from the ULTIMATE I & II Phase 3 Trials of Ublituximab in Multiple Sclerosis Presented at the American Academy of Neurology Annual Meeting

April 4, 2022

NEW YORK, April 04, 2022 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced data from the ULTIMATE I & II Phase 3 trials evaluating ublituximab in patients with relapsing forms of multiple sclerosis (RMS), presented over the weekend at the American Academy of Neurology (AAN) annual meeting, held in Seattle, Washington. Highlights of the presentations are outlined below.

Michael S. Weiss, Chairman and Chief Executive Officer of TG Therapeutics stated, “We are pleased to present additional analyses from the ULTIMATE I & II trials, which continue to highlight encouraging data for ublituximab as a potential treatment for patients with relapsing forms of multiple sclerosis. Of note, post hoc/pooled analyses demonstrate approximately 95% of ublituximab treated patients who demonstrated 12-week CDI sustained the improvement through the end of the study at week 96, a consistent NEDA benefit for ublituximab-treated patients was demonstrated across treatment epochs and key patient subpopulations, and 96% of patients completed their ublituximab infusions without interruptions.” Mr. Weiss continued, “We believe these data reinforce the potential of ublituximab, if approved, to offer RMS patients a treatment option that can be administered in a one-hour infusion every six months after the first dose.”

Poster Presentation Title: Disability Improvements With Ublituximab in Relapsing Multiple Sclerosis (RMS): Expanded Disability Status Scale (EDSS), 9-Hole Peg Test (9-HPT), and Timed 25-Foot Walk (T25FW) Evaluations From the Phase 3 ULTIMATE I and II Studies

- In pooled post hoc analyses of ULTIMATE I and II:
  - Among ublituximab patients who demonstrated 12-week Confirmed Disability Improvement (CDI), 95.4% (62/65) sustained the improvement through the end of the study at week 96.
  - In patients with a baseline Expanded Disability Status Score (EDSS) score ≥2.0, more patients in the ublituximab group than teriflunomide group had EDSS improvements of 1.0 and 1.5 points at Weeks 60, 72, 84, and 96 (P<0.05 for all)
  - At 96 weeks, a ≥20% improvement in 9-HPT was observed in 11.4% and 5.5% (dominant hand; P=0.0009) and 11.4% and 5.7% (nondominant hand; P=0.0016) of ublituximab (n=543) and teriflunomide (n=546) treated patients, respectively

Poster Presentation Title: Ublituximab Treatment Is Associated With a Significant Proportion of Patients Achieving No Evidence of Disease Activity (NEDA): Results From the Ultimate I and Ultimate II Phase 3 Studies of Ublituximab vs Teriflunomide in Relapsing Multiple Sclerosis (RMS)

- ULTIMATE I and II post hoc pooled analyses demonstrated a consistent NEDA benefit for ublituximab treated patients across treatment epochs and key patient subpopulations
- In pooled post hoc analyses evaluating NEDA-3 by treatment epoch and patient subtype:
  - NEDA-3 rates for ublituximab vs teriflunomide cohorts by treatment epoch at 0-96 weeks were 44.6% (232/520) vs 12.4% (65/524), respectively, and at 24-96 weeks (re-baselined) were 82.1% (418/509) vs 22.5% (115/511) (P<0.0001 for both)
  - NEDA-3 at 24-96 weeks (re-baselined) was achieved in 82.7% (268/324) vs 23.1% (81/350) of treatment-naive, 81.1% (34/161) vs 21.1% (150/185) of previously treated (prior disease-modifying therapy [DMT]), 82.4% (206/250) vs 18.6% (48/258) of early-disease, and 81.9% (212/259) vs 26.5% (67/253) of late-disease patients in ublituximab- vs teriflunomide-treated cohorts, respectively (P<0.0001 for all)
  - The leading cause of disease activity during Weeks 24-96 (re-baselined) was new/enlarging T2 lesions for teriflunomide (occurring in 71.6% of patients) and relapse for ublituximab (occurring in 11.4% of patients)

Poster Presentation Title: Infusion-Related Reactions (IRRs) With Ublituximab in Patients With Relapsing Multiple Sclerosis (RMS): Post Hoc Analyses From the Phase 3 ULTIMATE I and II Studies

- In pooled analyses of the ULTIMATE studies, 96.6% of patients (n=545) completed ublituximab infusions without interruption, and 94.6% completed Dose 2-5 maintenance infusions within 1 hour±5 minutes
- 43% of patients had an IRR at Dose 1, the proportion of patients experiencing an IRR markedly decreased to <10.0% for all subsequent infusions, and 69.5% did not have an IRR recurrence
- 78.8% of Dose 1 and 69.2% of Dose 2 IRRs with ublituximab occurred during the infusion period or within 1 hour post infusion
- The administration route of premedications (oral, intravenous [IV], intramuscular [IM], or mixed) did not impact the frequency of IRRs
- IRRs were the prevailing adverse event (AE) with ublituximab in ULTIMATE I and II; the vast majority were mild to

moderate in severity

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 the results of the ULTIMATE I & II Phase 3 studies and ublituximab as a potential treatment for 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 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; 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; and the uncertainties inherent in research and development. 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, 2021 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

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.