TG Therapeutics Announces Data for Ublituximab in Multiple Sclerosis Presented at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis

October 14, 2021

New ULTIMATE I & II data presented at ECTRIMS shows ublituximab treatment is associated with significant improvement in the multiple sclerosis functional composite (MSFC) score

Data from the ULTIMATE I & II Phase 3 trials recently supported a BLA submission to the U.S. FDA for ublituximab to treat patients with RMS

Webcast with key opinion leaders/investigators to be held today, Thursday, October 14, 2021 at 12:30 PM ET

NEW YORK, Oct. 14, 2021 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced data presentations, including additional analyses from two global, active-controlled, Phase 3 studies, called ULTIMATE I & II, evaluating ublituximab, the Company's investigational novel, glycoengineered anti-CD20 monoclonal antibody, compared to teriflunomide, in patients with relapsing forms of multiple sclerosis (RMS). As previously reported, both studies 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). During the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) additional data were presented in two presentations. Highlights from each presentation are included below.

Michael S. Weiss, Chairman and Chief Executive Officer of TG Therapeutics stated, "We are excited to share additional data from the ULTIMATE I & II trials during the ECTRIMS 2021 conference. The data further elucidate the potential benefits of ublituximab treatment especially on the tertiary endpoint of improvement in MSFC score, a detailed review of which is the subject of a late breaking e-poster.. We look forward to today's event and hope you all can join us and hear from the key opinion leaders."

The presentations at the 37th Congress of ECTRIMS highlighted the data from the ULTIMATE I & II Phase 3 trials including new additional analyses. These 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 ULTIMATE I & II trials were conducted under a Special Protocol Assessment (SPA) agreement with the U.S. Food and Drug Administration (FDA) and formed the basis for a Biologics License Application (BLA) submission for ublituximab in RMS which was submitted late last month. Highlights from each presentation, and links to the data presentations, are included below.

Oral Presentation Title: Phase 3 results of the ULTIMATE I & II global studies: ublituximab versus teriflunomide in relapsing multiple sclerosis

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 showed a 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 100% improvement in 12-week CDI (12% v. 6%; $p=0.0003$), and an 88% improvement in 24-week CDI (9.6% v. 5.1%; $p=0.0026$) compared to teriflunomide.

Additional Results

- A post-hoc analysis of the slopes from week 24 – week 96 showed there was no difference in the brain volume decline between the arms in ULTIMATE I and the rate of brain volume decline was lower for ublituximab in ULTIMATE II.
- In a prespecified analysis, ublituximab treatment was associated with significant improvement in Multiple Sclerosis Functional Composite (MSFC) score as compared to teriflunomide in both ULTIMATE I and II.

Safety/Tolerability

- 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).

Late Breaking ePoster Title: Ublituximab is associated with significant improvement in the multiple sclerosis functional composite (MSFC): results from the Phase 3 ULTIMATE I & II studies

- Improvements in disability were observed with ublituximab in both ULTIMATE I and II studies, with significantly more patients achieving 12-week or 24-week CDI vs teriflunomide
- In the prespecified analyses, ublituximab treatment was associated with significant improvement in MSFC score vs teriflunomide in both ULTIMATE I and II; this was driven by improvements in disability as measured by the 9-Hole Peg Test (9-HPT) and Timed 25-Foot Walk (T25FW)
- Further analyses of the effects of ublituximab on disability improvement in patients with RMS are ongoing

INVESTOR & ANALYST VIRTUAL EVENT INFORMATION
The Company will host a virtual event today, Thursday, October 14, 2021, at 12:30 PM ET, to discuss the ULTIMATE I & II Phase 3 data presented during the ECTRIMS meeting.

To attend the live event, please visit the Events page, located within the Investors & Media section, of the Company's website at http://ir.tgtherapeutics.com/events. Following the live event, an archive file will be available for replay, for a period of 30 days after the call.

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.

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 potential of ublituximab as a treatment for relapsing forms of multiple sclerosis.

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 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 FDA will not accept the Biologics License Application for ublituximab as a treatment for RMS that the Company submitted; 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

---

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.