TG Therapeutics Announces Results from the ULTIMATE I & II Phase 3 Trials of Investigational Ublituximab in RMS Published in The New England Journal of Medicine

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Ublituximab is an investigational targeted B-cell therapy that shows superior efficacy when compared with teriflunomide, a commonly prescribed oral treatment for multiple sclerosis

ULTIMATE I and II demonstrated significant reductions in risk of relapses, as well as reduction of active or new brain lesions

The US Food and Drug Administration and European Medicines Agency are currently reviewing marketing applications for ublituximab for the treatment of relapsing forms of multiple sclerosis (RMS) in adults

If approved, ublituximab will be the first B-cell therapy for use in RMS patients that can be given as a 1- hour infusion every 6 months, following the first dose

NEW YORK, Aug. 25, 2022 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced results from the ULTIMATE I & II Phase 3 trials evaluating ublituximab, the Company's investigational anti-CD20 monoclonal antibody, in patients with relapsing forms of multiple sclerosis (RMS), were published in The New England Journal of Medicine (NEJM).

Michael S. Weiss, Chairman and Chief Executive Officer of TG Therapeutics stated, "We are extremely pleased that the results from the ULTIMATE I & II trials have been published in The New England Journal of Medicine. We believe ublituximab's novel mechanism of action, coupled with the convenience of a one-hour infusion represents a potential advance for patients with RMS and we are pleased that this publication will share the ULTIMATE I and II data with a broad audience. We continue to be singularly focused on working toward the potential approval of ublituximab by the December 28, 2022 PDUFA goal date, and if successful, being prepared to launch early next year. We once again want to thank the patients that participated in ULTIMATE I and II and the healthcare providers at the sites that worked so hard on these trials."

Lawrence Steinman, MD, Zimmermann Professor of Neurology & Neurological Sciences, and Pediatrics at Stanford University and Global Study Chair for the ULTIMATE I & II trials stated, "The ULTIMATE trials found ublituximab treatment, compared to teriflunomide, produced significantly lower annualized relapse rates, reduction in the total number of MRI-detectable lesions, as well as improved rates of patients achieving no evidence of disease activity (NEDA). If approved, the unique attributes of ublituximab, particularly its ability to be infused in a one-hour infusion every six months following the first dose, may offer benefits to patients with relapsing forms of multiple sclerosis."

Key Data from the ULTIMATE I & II Trials

Primary Endpoint: Annualized Relapse Rate (ARR) Results

- In ULTIMATE I, treatment with ublituximab resulted in an ARR of 0.08 (n=271), compared to 0.19 for teriflunomide (n=274), (p<0.001).
- In ULTIMATE II, treatment with ublituximab resulted in an ARR of 0.09 (n=272), compared to 0.18 for teriflunomide (n=272), (p=0.002).

MRI Results

- In the ULTIMATE I trial, the mean total number of gadolinium enhancing lesions per T1-weighted MRI scan was 0.02 in the ublituximab group and 0.49 in the teriflunomide group (rate ratio, 0.03; 95% CI, 0.02 to 0.06; P<0.001); in the ULTIMATE II trial, the corresponding numbers were 0.01 and 0.25 (rate ratio, 0.04; 95% CI, 0.02 to 0.06; P<0.001).
- In the ULTIMATE I trial, the mean total number of new or enlarging hyperintense lesions per T2-weighted MRI scan was 0.21 in the ublituximab group and 2.79 in the teriflunomide group (rate ratio, 0.08; 95% CI, 0.06 to 0.10; P<0.001); in the ULTIMATE II trial, the corresponding numbers were 0.28 and 2.83 (rate ratio, 0.10; 95% CI, 0.07 to 0.14; P<0.001).

No Evidence of Disease Activity (NEDA) Results

- In ULTIMATE I, NEDA was observed in 44.6% of ublituximab treated patients and in 15% of the teriflunomide treated patients. In ULTIMATE II, NEDA was observed in 43% of ublituximab treated patients and in 11.4% of teriflunomide treated patients.

Prespecified Pooled Disability Results

- In the prespecified pooled analysis, 5.2% of the participants in the ublituximab group had worsening of disability confirmed at 12 weeks, as compared with 5.9% of the participants in the teriflunomide group (hazard ratio, 0.84; 95% CI, 0.50 to

1.41; P = 0.51); 3.3% of the participants in the ublituximab group had worsening of disability confirmed at 24 weeks, as compared with 4.8% of the participants in the teriflunomide group (hazard ratio, 0.66; 95% CI, 0.36 to 1.21). These results were not considered to be significantly different between treatment groups.

- In the prespecified pooled tertiary analysis that was not included in the hierarchical analysis and from which no conclusions can be drawn, 12.0% of the participants who received ublituximab had lessening of disability confirmed at 12 weeks, as compared with 6.0% of the participants who received teriflunomide (hazard ratio, 2.16; 95% CI, 1.41 to 3.31); 9.6% of the participants who received ublituximab had lessening of disability confirmed at 24 weeks, as compared with 5.1% of the participants who received teriflunomide (hazard ratio, 2.03; 95% CI, 1.27 to 3.25).

Safety/Tolerability

- In a pooled analysis of the two trials, 486 of 545 participants (89.2%) who received ublituximab and 501 of 548 participants (91.4%) who received teriflunomide had at least one adverse event. Grade 3 or higher adverse events occurred in 116 participants (21.3%) who received ublituximab and in 77 (14.1%) who received teriflunomide.

- 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% for the teriflunomide group).

Based primarily on the results of the ULTIMATE I & II trials, marketing applications for ublituximab to treat patients with RMS have been accepted and are currently under review by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). As previously announced, ublituximab was granted a Prescription Drug Fee User Act (PDUFA) goal date of December 28, 2022 by the FDA.

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 teriflunomide 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
TG Therapeutics is a biopharmaceutical company focused on the acquisition, development and commercialization of novel treatments for B-cell diseases. In addition to a research pipeline including several investigational medicines, TG has completed a Phase 3 program for ublituximab, an investigational glycoengineered monoclonal antibody that targets a unique epitope on CD20-expressing B-cells, to treat patients with relapsing forms of multiple sclerosis (RMS). 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 FDA review of the Biologics License Application (BLA) for ublituximab for the treatment of relapsing forms of Multiple Sclerosis (RMS) and the commercial potential of ublituximab for the treatment of RMS if the BLA is approved.

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 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 ublituximab will not be commercially successful, if approved; 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 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; 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, 2021, our most recent Quarterly Report filed on Form 10-Q, and our other filings with the U.S. Securities and Exchange Commission. 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.