New Data for BRIUMVI® Demonstrate 89.9% of Patients with Relapsing Multiple Sclerosis Were Free from Disability Progression After 6 Years of Continuous BRIUMVI Treatment

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During year 6 of continuous treatment with BRIUMVI the annualized relapse rate was 0.012, equivalent to one relapse occurring every 83 years of patient treatment

Overall safety profile of BRIUMVI remained consistent over 6 years of continuous treatment, with no new safety signals emerging with prolonged treatment

NEW YORK, Sept. 24, 2025 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced updated data presentations including new six-year data from the ULTIMATE I & II Phase 3 trials evaluating BRIUMVI® (ublituximab-xiiy) in patients with relapsing forms of multiple sclerosis (RMS), at the 2025 European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) annual meeting, where we and our Ex-U.S. partner, Neuraxpharm, are exhibiting. Links to each presentation as well as highlights from the presentations are outlined below.

Bruce Cree, MD, PhD, MAS, Zimmermann Endowed Professor in Multiple Sclerosis, and Professor of Neurology at UCSF Weill Institute for Neurosciences, University of California, San Francisco stated, “The data for BRUIMVI at six years of continuous therapy provides compelling evidence of durable efficacy, with sustained protection against not only relapses but also disability progression. These data also underscore the benefit of early treatment with ublituximab compared to delayed treatment on disability outcomes. Furthermore, the consistency of outcomes in clinical trials compared with emerging data from observational studies is striking and strongly supports use of ublituximab in clinical practice.”

Michael S. Weiss, the Company’s Chairman and Chief Executive Officer stated, “We are extremely pleased to share six years of continuous BRIUMVI treatment data demonstrating that nearly 90% of patients on BRIUMVI remained free from disability progression, coupled with one of the lowest relapse rates ever reported in a Phase 3 RMS study. These results, together with the encouraging data from our ongoing ENHANCE dosing trial and the ENABLE real-world observational study, reinforce our confidence in BRIUMVI’s potential to deliver both meaningful efficacy and real-world convenience for people with RMS.”

TG PRESENTATIONS:

Oral Presentation: Long-term Efficacy and Safety of Ublituximab in Relapsing Multiple Sclerosis: Results from Six Years of ULTIMATE I and II Open-label Extension

- Patients on continuous BRIUMVI treatment exhibited low and decreasing annualized relapse rate (ARR) throughout the observation period, ARR: 0.053, 0.032, 0.020, and 0.012 for Years 3, 4, 5, and 6 respectively.
- After 6 years of continuous BRIUMVI treatment, 10.1% of patients had Confirmed Disability Progression (CDP) lasting 24 weeks compared to 15.9% of patients who switched from teriflunomide to BRIUMVI [HR (95% CI): 0.658; p=0.0238], and 89.9% remained progression free with continuous BRIUMVI treatment.
- 17% of patients treated with BRIUMVI continuously for 6 years achieved Confirmed Disability Improvement (CDI) lasting at least 24 weeks compared to 13.3% of patients who switched from teriflunomide to BRIUMVI [HR (95% CI): 1.414; p=0.0396].
- The overall safety profile of BRIUMVI remained consistent over 6 years of continuous treatment in an exposure-adjusted analysis of adverse events (AEs), with no new safety signals emerging with prolonged treatment.
- Immunoglobulin levels remained stable with prolonged BRIUMVI treatment, and the mean IgM and IgG levels remained above the lower limit of normal. There was no association between decreased immunoglobulin levels and risk of serious infections after 6 years of treatment.

ePoster Presentation: Safety and Tolerability of a Modified Ublituximab Dosing Regimen: Updates from the ENHANCE Study

- Consolidating Day 1 (150 mg) and Day 15 (450 mg) BRIUMVI infusions into a single 600 mg dose on Day 1 was well-tolerated across a range of infusion durations, from 1 hour to 4 hours.
- The 4 hour 600 mg BRIUMVI Day 1 infusion was associated with the lowest infusion related reaction (IRR) rate and is currently being evaluated in a double-blinded, randomized, label-enabling trial design compared to standard dosing.

ePoster Presentation: Real-World Clinical Experience from ENABLE: the First Phase 4 Observational Study for Patients with Relapsing Multiple Sclerosis Initiating Ublituximab

- These data demonstrate consistent clinical outcomes with previously conducted pivotal clinical studies. The cohort’s diversity along racial, ethnic, and geographic demographics, provides further understanding of real-world populations on BRIUMVI.
- On-treatment ARR was 0.015 in RMS patients (132.4 patient-years) transitioning to BRIUMVI in real-world clinical setting,

with 99.5% of participants reporting no relapses on BRIUMVI.
- Infusion durations in real-world were consistent with the expected infusion times.
- BRIUMVI was well tolerated in real-world clinical setting. IRRs were significantly lower compared to the pivotal ULTIMATE I & II studies.
- Significant improvements in patient-reported outcomes were observed at Day 15 (2nd infusion) and week 24 (3rd infusion).
- The overall safety profile remained consistent in observational study compared to ULTIMATE I and II.

Following the presentations, the data presented will be 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 & II are two randomized, double-blind, double-dummy, parallel group, active comparator-controlled clinical trials of identical design, in patients with RMS treated for 96 weeks. Patients were randomized to receive either BRIUMVI, given as an IV infusion of 150 mg administered in four hours, 450 mg two weeks after the first infusion administered in one hour, and 450 mg every 24 weeks administered in one hour, with oral placebo administered daily; or teriflunomide, the active comparator, given orally as a 14 mg daily dose with IV placebo administered on the same schedule as BRIUMVI. Both studies enrolled patients who had experienced at least one relapse in the previous year, two relapses in the previous two years, or had the presence of a T1 gadolinium (Gd)-enhancing lesion in the previous year. Patients were also required to have an Expanded Disability Status Scale (EDSS) score from 0 to 5.5 at baseline. 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. Additional information on these clinical trials can be found at www.clinicaltrials.gov (NCT03277261; NCT03277248).

ABOUT BRIUMVI® (ublituximab-xiiy) 150 mg/6 mL Injection for IV
BRIUMVI is a novel monoclonal antibody that targets a unique epitope on CD20-expressing B-cells. Targeting CD20 using monoclonal antibodies has proven to be an important therapeutic approach for the management of autoimmune disorders, such as RMS. BRIUMVI is uniquely designed to lack certain sugar molecules normally expressed on the antibody. Removal of these sugar molecules, a process called glycoengineering, allows for efficient B-cell depletion at low doses.

BRIUMVI is indicated in the U.S. for the treatment of adults with RMS, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease and in the EU and UK for the treatment of adult patients with RMS with active disease defined by clinical or imaging features.

A list of authorized specialty distributors can be found at www.briumvi.com.

IMPORTANT SAFETY INFORMATION
Contraindications: BRIUMVI is contraindicated in patients with:

- Active Hepatitis B Virus infection
- A history of life-threatening infusion reaction to BRIUMVI

WARNINGS AND PRECAUTIONS

Infusion Reactions: BRIUMVI can cause infusion reactions, which can include pyrexia, chills, headache, influenza-like illness, tachycardia, nausea, throat irritation, erythema, and an anaphylactic reaction. In MS clinical trials, the incidence of infusion reactions in BRIUMVI-treated patients who received infusion reaction-limiting premedication prior to each infusion was 48%, with the highest incidence within 24 hours of the first infusion. 0.6% of BRIUMVI-treated patients experienced infusion reactions that were serious, some requiring hospitalization.

Observe treated patients for infusion reactions during the infusion and for at least one hour after the completion of the first two infusions unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion. Inform patients that infusion reactions can occur up to 24 hours after the infusion. Administer the recommended pre-medication to reduce the frequency and severity of infusion reactions. If life-threatening, stop the infusion immediately, permanently discontinue BRIUMVI, and administer appropriate supportive treatment. Less severe infusion reactions may involve temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

Infections: Serious, life-threatening or fatal, bacterial and viral infections have been reported in BRIUMVI-treated patients. In MS clinical trials, the overall rate of infections in BRIUMVI-treated patients was 56% compared to 54% in teriflunomide-treated patients. The rate of serious infections was 5% compared to 3% respectively. There were 3 infection-related deaths in BRIUMVI-treated patients. The most common infections in BRIUMVI-treated patients included upper respiratory tract infection (45%) and urinary tract infection (10%). Delay BRIUMVI administration in patients with an active infection until the infection is resolved.

Consider the potential for increased immunosuppressive effects when initiating BRIUMVI after immunosuppressive therapy or initiating an immunosuppressive therapy after BRIUMVI.

Hepatitis B Virus (HBV) Reactivation: HBV reactivation occurred in an MS patient treated with BRIUMVI in clinical trials. Fulminant hepatitis, hepatic failure, and death caused by HBV reactivation have occurred in patients treated with anti-CD20 antibodies. Perform HBV screening in all patients before initiation of treatment with BRIUMVI. Do not start treatment with BRIUMVI in patients with active HBV confirmed by positive results for HB surface antigen (HBsAg) and anti-HB tests. For patients who are negative for HBsAg and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult a liver disease expert before starting and during treatment.

Progressive Multifocal Leukoencephalopathy (PML): Although no cases of PML have occurred in BRIUMVI-treated MS patients, JC virus infection resulting in PML has been observed in patients treated with other anti-CD20 antibodies and other MS therapies.

If PML is suspected, withhold BRIUMVI and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

MRI findings may be apparent before clinical signs or symptoms; monitoring for signs consistent with PML may be useful. Further investigate suspicious findings to allow for an early diagnosis of PML, if present. Following discontinuation of another MS medication associated with PML, lower PML-related mortality and morbidity have been reported in patients who were initially asymptomatic at diagnosis compared to patients who had characteristic clinical signs and symptoms at diagnosis.

If PML is confirmed, treatment with BRIUMVI should be discontinued.

Vaccinations: Administer all immunizations according to immunization guidelines: for live or live-attenuated vaccines, at least 4 weeks and, whenever possible, at least 2 weeks prior to initiation of BRIUMVI for non-live vaccines. BRIUMVI may interfere with the effectiveness of non-live vaccines. The safety of immunization with live or live-attenuated vaccines during or following administration of BRIUMVI has not been studied. Vaccination with live virus vaccines is not recommended during treatment and until B-cell repletion.

Vaccination of Infants Born to Mothers Treated with BRIUMVI During Pregnancy: In infants of mothers exposed to BRIUMVI during pregnancy, assess B-cell counts prior to administration of live or live-attenuated vaccines as measured by CD19+ B-cells. Depletion of B-cells in these infants may increase the risks from live or live-attenuated vaccines. Inactivated or non-live vaccines may be administered prior to B-cell recovery. Assessment of vaccine immune responses, including consultation with a qualified specialist, should be considered to determine whether a protective immune response was mounted.

Fetal Risk: Based on data from animal studies, BRIUMVI may cause fetal harm when administered to a pregnant woman. Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 B-cell depleting antibodies during pregnancy. Advise females of reproductive potential to use effective contraception during BRIUMVI treatment and for 6 months after the last dose.

Reduction in Immunoglobulins: As expected with any B-cell depleting therapy, decreased immunoglobulin levels were observed. Decrease in immunoglobulin M (IgM) was reported in 0.6% of BRIUMVI-treated patients compared to none of the patients treated with teriflunomide in RMS clinical trials. Monitor the levels of quantitative serum immunoglobulins during treatment, especially in patients with opportunistic or recurrent infections, and after discontinuation of therapy, until B-cell repletion. Consider discontinuing BRIUMVI therapy if a patient with low immunoglobulins develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

Liver Injury: Clinically significant liver injury, without findings of viral hepatitis, has been reported in the postmarketing setting in patients treated with anti-CD20 B-cell depleting therapies approved for the treatment of MS, including BRIUMVI. Signs of liver injury, including markedly elevated serum hepatic enzymes with elevated total bilirubin, have occurred from weeks to months after administration.

Patients treated with BRIUMVI found to have an alanine aminotransaminase (ALT) or aspartate aminotransferase (AST) greater than 3x the upper limit of normal (ULN) with serum total bilirubin greater than 2x ULN are potentially at risk for severe drug-induced liver injury.

Obtain liver function tests prior to initiating treatment with BRIUMVI, and monitor for signs and symptoms of any hepatic injury during treatment. Measure serum aminotransferases, alkaline phosphatase, and bilirubin levels promptly in patients who report symptoms that may indicate liver injury, including new or worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice. If liver injury is present and an alternative etiology is not identified, discontinue BRIUMVI.

Most Common Adverse Reactions: The most common adverse reactions in RMS trials (incidence of at least 10%) were infusion reactions and upper respiratory tract infections.

Physicians, pharmacists, or other healthcare professionals with questions about BRIUMVI should visit www.briumvi.com.

The full Summary of Product Characteristics approved in the European Union (EU) for BRIUMVI can be found here Briumvi | European Medicines Agency (europa.eu).

ABOUT BRIUMVI PATIENT SUPPORT in the U.S.
BRIUMVI Patient Support is a flexible program designed by TG Therapeutics to support U.S. patients through their treatment journey in a way that works best for them. More information about the BRIUMVI Patient Support program can be accessed at www.briumvipatientsupport.com.

ABOUT TG THERAPEUTICS
TG Therapeutics is a fully integrated, commercial stage, 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 Therapeutics has received approval from the U.S. Food and Drug Administration (FDA) for BRIUMVI® (ublituximab-xiiy) for the treatment of adult patients with relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, as well as approval by the European Commission (EC) in Europe, the Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom, Swissmedic in Switzerland, and Australia's Therapeutic Goods Administration (TGA) for BRIUMVI to treat adult patients with RMS who have active disease defined by clinical or imaging features. For more information, visit www.tgtherapeutics.com, and follow us on X (formerly Twitter) @TGTherapeutics and on LinkedIn.

BRIUMVI® 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.

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 below.

Such forward looking statements include but are not limited to statements regarding the results of the long term safety and efficacy from the ULTIMATE I & II Phase 3 studies, the ENHANCE Phase 3b study, the ENABLE Phase 4 Observational Study, and BRIUMVI as a treatment for relapsing forms of multiple sclerosis (RMS). Additional factors that could cause our actual results to differ materially include the following: the risk that

the data from the ULTIMATE I & II long term open label extension, ENHANCE, or ENABLE trials that we announce or publish may change, or the product profile of BRIUMVI 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 safety and tolerability profile and commercial potential of BRIUMVI; the risk that any individual patient's clinical experience in the post-marketing setting, or the aggregate patient experience in the post-marketing setting, may differ from that demonstrated in controlled clinical trials such as ULTIMATE I and II; our ability to successfully market and sell BRIUMVI in RMS; 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 BRIUMVI, and the ability of the Company and its manufacturers and suppliers to produce and deliver BRIUMVI to meet the market demand for BRIUMVI; the failure to obtain and maintain requisite regulatory approvals, including the risk that the Company fails to satisfy post-approval regulatory requirements; the uncertainties inherent in research and development; and general political, economic and business conditions. 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, 2024 and in 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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