



TG Therapeutics Announces Publication of Five-Year Comparative Analysis of BRIUMVI Versus Ocrelizumab and Ofatumumab in Relapsing Multiple Sclerosis

October 12, 2026

BRIUMVI was associated with a lower risk of 24-week confirmed disability progression and lower annualized relapse rates (ARRs) over five years compared with ocrelizumab and ofatumumab

NEW YORK--(BUSINESS WIRE)--Oct. 12, 2026-- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced the publication of results from a five-year matching-adjusted indirect comparison (MAIC) evaluating long-term relapse activity and disability progression outcomes with BRIUMVI® (ublituximab-xiyy) compared with ocrelizumab and ofatumumab in patients with relapsing multiple sclerosis (RMS). For the analysis, individual patient data from the Phase 3 ULTIMATE I/II pivotal trials for BRIUMVI were reweighted to match published baseline characteristics from the pivotal studies for ocrelizumab and ofatumumab in patients with RMS, revealing favorable long-term outcomes with BRIUMVI compared to the other two comparators. The manuscript, entitled "*Long-Term Comparative Outcomes in Relapse Activity and Disability Progression Among Anti-CD20 Therapies in Relapsing Multiple Sclerosis: An Unanchored Matching-Adjusted Indirect Comparison*," was published online in *Multiple Sclerosis and Related Disorders*.

Michael S. Weiss, Chairman and Chief Executive Officer of TG Therapeutics, stated, "In an era where physicians and patients are fortunate to have multiple anti-CD20 treatment options available for relapsing MS, the lack of comparative data makes choosing the right one challenging. This is particularly important for people living with a chronic disease like MS, where preventing the accumulation of disability over time is an important treatment goal."

Mr. Weiss continued, "In the absence of head-to-head clinical trials, MAIC provides a valuable statistical approach to evaluating comparative treatment outcomes while accounting for differences in patient populations across studies. We are encouraged that this analysis showed that BRIUMVI was associated with consistently lower relapse activity versus ocrelizumab and a lower risk of confirmed disability progression compared with both ocrelizumab and ofatumumab over five years. We believe these findings add to the growing body of evidence supporting the durable efficacy profile of BRIUMVI and its potential to provide meaningful long-term benefit for people living with MS."

The manuscript can be accessed at [ScienceDirect.com](https://www.sciencedirect.com) or on the publications page of the TG corporate website at www.tgtherapeutics.com/publications/.

Key Findings from the Publication

Five-year anti-CD20 outcomes from the pivotal studies of BRIUMVI, ocrelizumab, and ofatumumab were compared using an unanchored MAIC (see below for more information about the MAIC). The analysis used individual patient-level data from 545 BRIUMVI (ublituximab)-treated participants in the Phase 3 ULTIMATE I and II trials and their open-label extension and compared outcomes with published aggregate data from the Phase 3 OPERA I/II trials of ocrelizumab and ASCLEPIOS I/II trials of ofatumumab. In the analysis, BRIUMVI patient-level data were re-weighted to align baseline characteristics with the respective comparator trial populations. These adjustments are designed to mitigate the effects of any demographic differences in the study populations on the efficacy results.

The findings included:

- BRIUMVI was associated with a lower risk of 24-week confirmed disability progression (CDP24) compared with both ocrelizumab and ofatumumab, with a 44% lower relative hazard versus ocrelizumab (HR 0.560; 95% CI: 0.380–0.826) and a 49% lower relative hazard versus ofatumumab (HR 0.509; 95% CI: 0.350–0.741).
- BRIUMVI was associated with a lower cumulative incidence of CDP24 at 240 weeks, with estimated rates of 9.3% versus 16.1% for ocrelizumab and 9.4% versus 17.9% for ofatumumab.
- BRIUMVI was associated with more time free from confirmed disability progression over 240 weeks, with an average of 8.1 additional weeks compared with ocrelizumab (95% CI: 2.3–14.1) and 13.1 additional weeks compared with ofatumumab (95% CI: 6.7–19.3).
- BRIUMVI demonstrated consistently low annualized relapse rates (ARR) over five years of treatment, with MAIC-adjusted ARR declining from 0.118 in Year 1 to 0.032 in Year 5 in the comparison with ocrelizumab, and from 0.116 to 0.030 in the comparison with ofatumumab.
- These findings are considered exploratory and require confirmation in direct comparative studies.

About the MAIC Analysis

In the absence of randomized head-to-head trials directly comparing anti-CD20 therapies in RMS, investigators conducted an unanchored MAIC to explore comparative outcomes over five years. Individual patient data from the pivotal Phase 3 ULTIMATE I and II studies were reweighted to match published baseline characteristics from the pivotal Phase 3 studies for ocrelizumab (OPERA I/II) and ofatumumab (ASCLEPIOS I/II), including age, sex, baseline Expanded Disability Status Scale (EDSS) score, gadolinium-enhancing lesion prevalence, T2 lesion volume, prior relapse activity and time since diagnosis, where corresponding data were available. Following weighting, baseline characteristics were closely aligned with both comparator populations.

The authors note that the findings should be interpreted within the inherent limitations of an unanchored MAIC. Notably, the methodology cannot

adjust for unmeasured differences between trials, and residual confounding cannot be excluded. Accordingly, the analysis is exploratory and the findings require confirmation through direct comparative studies or robust real-world evidence.

The study was funded by Neuraxpharm, TG Therapeutics' European commercialization partner for BRIUMVI.

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 TG THERAPEUTICS

TG Therapeutics is a fully integrated, commercial stage, biotechnology company focused on the acquisition, development and commercialization of novel treatments for B-cell diseases. In addition to a research pipeline, TG Therapeutics has received approval from the U.S. Food and Drug Administration (FDA) for BRIUMVI® (ublituximab-xiyy) to treat adult patients with relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, as well as approval from several regulatory agencies outside of the U.S. 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](https://twitter.com/TGTherapeutics) and on [LinkedIn](https://www.linkedin.com/company/tgtherapeutics).

BRIUMVI® is a registered trademark of TG Therapeutics, Inc.

ABOUT BRIUMVI® (ublituximab-xiyy) 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 several countries outside of the U.S. 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): PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. JCV infection resulting in PML has been

observed in patients treated with anti-CD20 antibodies, including BRIUMVI, 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.

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 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

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 potential significance and implications of the published results; the potential for BRIUMVI (ublituximab-xiyy) to provide meaningful long-term benefit for people living with relapsing multiple sclerosis (RMS); the potential for the published findings to support the efficacy profile, differentiation, utilization, acceptance or commercial opportunity for BRIUMVI;

and expectations regarding the continued commercialization, healthcare professional and patient acceptance, and use of BRIUMVI in the United States and jurisdictions outside the United States.

Additional factors that could cause actual results to differ materially include: the inherent limitations of matching-adjusted indirect comparisons and other cross-trial analyses; the risk that the results of the analysis may not be confirmed in other clinical studies or real-world evidence; the risk that differences in trial design, patient populations, treatment exposure, follow-up, unmeasured or unavailable prognostic factors, treatment effect modifiers, or other sources of residual confounding may affect the interpretation of the results; the risk that the results may not be indicative of outcomes in broader patient populations or clinical practice; and the uncertainties generally inherent in research and development and the interpretation of clinical and comparative effectiveness data.

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.

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.

View source version on [businesswire.com](https://www.businesswire.com/news/home/20261012952834/en/): <https://www.businesswire.com/news/home/20261012952834/en/>

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

Source: TG Therapeutics, Inc.