TG Therapeutics Announces Launch of the ULTRA-V Phase 3 Trial Evaluating the Triple Combination of UKONIQ™ (umbralisib), Ublituximab, and Venetoclax

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ULTRA-V Phase 2 trial has reached completion of patient enrollment

NEW YORK, April 21, 2021 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced the initiation of patient enrollment into the ULTRA-V Phase 3 randomized trial, evaluating the time-limited triple combination of UKONIQ™ (umbralisib), the Company's once-daily, inhibitor of PI3K-delta and CK1-epsilon, ublituximab, the Company's investigational glycoengineered anti-CD20 monoclonal antibody, and venetoclax, compared to the continuous doublet combination of UKONIQ plus ublituximab (U2) in patients with both frontline and relapsed or refractory chronic lymphocytic leukemia (CLL). The primary endpoint for the ULTRA-V Phase 3 trial is Progression-free Survival (PFS), and the trial is designed support the full approval of the triple combination of U2 plus venetoclax.

The Company also announced completion of enrollment into the ULTRA-V Phase 2 global, single arm trial evaluating the triple combination of U2 plus venetoclax. This primary endpoint for this trial is overall response rate (ORR) and complete response (CR) rate, and the trial completed enrollment with approximately 165 patients enrolled. The trial enrolled patients with front line CLL, as well as relapsed or refractory CLL, including patients who were refractory to prior Bruton's Kinase Inhibitor (BTK) therapy.

Richard R. Furman, MD, Director of CLL Research Center at Weill Cornell Medicine and Study Chair for the ULTRA-V Phase 2 and Phase 3 trials stated, "We are excited to launch this pivotal Phase 3 study based on the promising Phase 1 clinical results reported to date on the triplet combination of UKONIQ, ublituximab and venetoclax in patients with CLL. While recent approvals provide excellent treatment options for patients, disease progression and treatment tolerability still remain problematic for many patients. Our belief is that time-limited treatment regimens, such as U2 plus venetoclax, have the potential to produce meaningful responses without the need to expose patients to continuous therapy and related toxicities. We look forward to presenting the results of the Phase 2 portion of this study at a future medical meeting. I want to thank my colleagues for their strong support of the Phase 2 ULTRA-V trial and look forward to continuing and expanding our efforts now in Phase 3."

Michael S. Weiss, Executive Chairman and Chief Executive Officer of TG Therapeutics stated, "We are extremely pleased with the rapid enrollment seen in the ULTRA-V Phase 2 trial, with approximately 165 patients enrolled in approximately 16 months throughout a limited number of U.S. trial sites, with the majority of the enrollment taking place in 2020 during the height of the COVID-19 pandemic. We are further encouraged by the strong interest of new trial sites to participate in the Phase 3 portion of the trial. We believe the encouraging early results observed in the Phase 1 trial of U2 plus venetoclax, led by Dr. Paul Barr at the University of Rochester, which were most recently presented at the ASH annual meeting in 2020, are supportive of our decision to quickly initiate the ULTRA-V Phase 2 and 3 trials. We look forward to providing an update from the Phase 1 trial later this year and initial results from the Phase 2 portion of the ULTRA-V trial in 2022."

ABOUT ULTRA-V PHASE 3 TRIAL
The ULTRA-V Phase 3 trial is an open-label, multicenter, randomized controlled clinical trial comparing the time-limited triple combination of UKONIQ and ublituximab (U2) plus venetoclax, to an active control arm of continuous U2. The Phase 3 trial includes two independent randomized cohorts of CLL subjects: a treatment-naïve cohort and a previously treated cohort, with each cohort being enrolled and evaluated independently of each other. The primary endpoint for the trial is Progression-free Survival (PFS). This trial is being led by Richard R. Furman, MD, Director of CLL Research Center at Weill Cornell Medicine and targeting over 60 U.S. trial sites.

ABOUT ULTRA-V PHASE 2 TRIAL
The ULTRA-V Phase 2 trial, (NCT03801525), is an open-label, multicenter, trial designed to investigate the efficacy and safety of ublituximab and UKONIQ combined with venetoclax in subjects with CLL. The primary endpoint of the trial is overall response rate (ORR) and Complete Response (CR) rate. The trial enrolled approximately 165 patients with front line and previously treated CLL at 26 sites throughout the United States.

ABOUT U2 PLUS VENETOCLAX PHASE 1 TRIAL
The Phase 1/2 trial, (NCT03379051), is a multi-center, dose-escalation trial designed to assess the safety and efficacy of U2 plus venetoclax in patients with relapsed or refractory CLL. The primary objective of the trial is to evaluate the safety of venetoclax after U2 induction. The secondary objectives are clinical efficacy as defined by ORR (including CR rate), PFS, and undetectable minimal residual disease (MRD) rate after 12 cycles of therapy. The trial enrolled approximately 50 CLL patients, and interim results were most recently presented on 43 CLL patients at the American Society of Hematology (ASH) annual meeting in December 2020.

ABOUT CHRONIC LYMPHOCYTIC LEUKEMIA
Chronic lymphocytic leukemia (CLL) is the most common type of adult leukemia. It is estimated there will be more than 20,000 new cases of CLL diagnosed in the United States in 2020 and approximately 45,000 new cases globally in 2020.[1,2] Although signs and symptoms of CLL may disappear for a period of time after initial treatment, the disease is considered incurable and many people will require additional treatment due to the return of malignant cells.

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 two 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 trademark of TG Therapeutics, Inc.

ABOUT UKONIQ™(umbralisib)
UKONIQ is the first and only oral inhibitor of phosphoinositide 3 kinase (PI3K) delta and casein kinase 1 (CK1) epsilon. PI3K-delta is known to play an important role in supporting cell proliferation and survival, cell differentiation, intercellular trafficking and immunity and is expressed in both normal and malignant B-cells. CK1-epsilon is a regulator of oncoprotein translation and has been implicated in the pathogenesis of cancer cells, including lymphoid malignancies.

UKONIQ is indicated for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen and for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy.

These indications are approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

IMPORANT SAFETY INFORMATION
Infections: Serious, including fatal, infections occurred in patients treated with UKONIQ. Grade 3 or higher infections occurred in 10% of 335 patients, with fatal infections occurring in <1% . The most frequent Grade ≥3 infections included pneumonia, sepsis, and urinary tract infection. Provide prophylaxis for *Pneumocystis jirovecii* pneumonia (PJP) and consider prophylactic antivirals during treatment with UKONIQ to prevent CMV infection, including CMV reactivation. Monitor for any new or worsening signs and symptoms of infection, including suspected PJP or CMV, during treatment with UKONIQ. For Grade 3 or 4 infection, withhold UKONIQ until infection has resolved. Resume UKONIQ at the same or a reduced dose. Withhold UKONIQ in patients with suspected PJP of any grade and permanently discontinue in patients with confirmed PJP. For clinical CMV infection or viremia, withhold UKONIQ until infection or viremia resolves. If UKONIQ is resumed, administer the same or reduced dose and monitor patients for CMV reactivation by PCR or antigen test at least monthly.

Neutropenia: Serious neutropenia occurred in patients treated with UKONIQ. Grade 3 neutropenia developed in 9% of 335 patients and Grade 4 neutropenia developed in 9%. Monitor neutrophil counts at least every 2 weeks for the first 2 months of UKONIQ and at least weekly in patients with neutrophil count <1 x 10^9/L (Grade 3-4) neutropenia during treatment with UKONIQ. Consider supportive care as appropriate. Withhold, reduce dose, or discontinue UKONIQ depending on the severity and persistence of neutropenia.

Diarrhea or Non-Infectious Colitis: Serious diarrhea or non-infectious colitis occurred in patients treated with UKONIQ. Any grade diarrhea or colitis occurred in 53% of 335 patients and Grade 3 occurred in 9%. For patients with severe diarrhea (Grade 3, i.e., > 6 stools per day over baseline) or abdominal pain, stool with mucus or blood, change in bowel habits, or peritoneal signs, withhold UKONIQ until resolved and provide supportive care with antidiarrheals or enteric acting steroids as appropriate. Upon resolution, resume UKONIQ at a reduced dose. For recurrent Grade 3 diarrhea or recurrent colitis of any grade, discontinue UKONIQ. Discontinue UKONIQ for life-threatening diarrhea or colitis.

Hepatotoxicity: Serious hepatotoxicity occurred in patients treated with UKONIQ. Grade 3 and 4 transaminase elevations (ALT and/or AST) occurred in 8% and <1%, respectively, in 335 patients. Monitor hepatic function at baseline and during treatment with UKONIQ. For ALT/AST greater than 5 to less than 20 times ULN, withhold UKONIQ until return to less than 3 times ULN, then resume at a reduced dose. For ALT/AST elevation greater than 20 times ULN, discontinue UKONIQ.

Severe Cutaneous Reactions: Severe cutaneous reactions, including a fatal case of exfoliative dermatitis, occurred in patients treated with UKONIQ. Grade 3 cutaneous reactions occurred in 2% of 335 patients and included exfoliative dermatitis, erythema, and rash (primarily maculo-papular). Monitor patients for new or worsening cutaneous reactions. Review all concomitant medications and discontinue any potentially contributing medications. Withhold UKONIQ for severe (Grade 3) cutaneous reactions until resolution. Monitor at least weekly until resolved. Upon resolution, resume UKONIQ at a reduced dose. Discontinue UKONIQ if severe cutaneous reaction does not improve, worsens, or recurs. Discontinue UKONIQ for life-threatening cutaneous reactions or SJS, TEN, or DRESS of any grade. Provide supportive care as appropriate.

Allergic Reactions Due to Inactive Ingredient FD&C Yellow No. 5: UKONIQ contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons, frequently in patients who also have aspirin hypersensitivity.

Embryo-fetal Toxicity: Based on findings in animals and its mechanism of action, UKONIQ can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females and males with female partners of reproductive potential to use effective contraception during treatment and for at least one month after the last dose.

Serious adverse reactions occurred in 18% of 221 patients who received UKONIQ. Serious adverse reactions that occurred in ≥2% of patients were diarrhea-colitis (4%), pneumonia (3%), sepsis (2%), and urinary tract infection (2%). Permanent discontinuation of UKONIQ due to an adverse reaction occurred in 14% of patients. Dose reductions of UKONIQ due to an adverse reaction occurred in 11% of patients. Dosage interruptions of UKONIQ due to an adverse reaction occurred in 43% of patients.

The most common adverse reactions (>15%), including laboratory abnormalities, in 221 patients who received UKONIQ were increased creatinine (79%), diarrhea-colitis (58%, 2%), fatigue (41%), nausea (38%), neutropenia (33%), ALT increase (33%), AST increase (32%), musculoskeletal pain (27%), anemia (27%), thrombocytopenia (26%), upper respiratory tract infection (21%), vomiting (21%), abdominal pain (19%), decreased appetite (19%), and rash (18%).

Lactation: Because of the potential for serious adverse reactions from umbralisib in the breastfed child, advise women not to breastfeed during

treatment with UKONIQ and for at least one month after the last dose.

Please visit www.tgtherapeutics.com/prescribing-information/uspi-ukon for full Prescribing Information and Medication Guide.

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[1] Cancer Stat Facts: Leukemia — Chronic Lymphocytic Leukemia (CLL). National Cancer Institute Surveillance, Epidemiology, and End Results Program website. https://seer.cancer.gov/statfacts/html/clyl.html. Accessed October 26, 2020.

[2] EpiCast Report: Chronic Lymphocytic Leukemia – Epidemiology Forecast to 2025. Available at: https://store.globaldata.com/report/gdhcer164-17–epicast-report-chronic-lymphocytic-leukemia-epidemiology-forecast-to-2025/.

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 U.S. Private Securities Litigation Reform Act of 1995. Such forward-looking statements include but are not limited to statements regarding the expectations and plans for the clinical trials evaluating UKONIQ™(umbralisib) and ublituximab (U2) in combination with venetoclax, the availability of results from those trials, and the potential of U2 in combination with venetoclax as a treatment for CLL.

In addition to the risk factors identified from time to time in our reports filed with the U.S. Securities and Exchange Commission, factors that could cause our actual results to differ materially are the following: the risk that we will not be able to meet the clinical trial or regulatory submission timelines that we project or achieve other anticipated milestones; the risk that interim, top-line, or other early clinical trial results, that may have influenced our decision to proceed with additional clinical trials, including the clinical studies evaluating U2 in combination with venetoclax, will not be reproduced in final data sets or in future studies; the risk that the safety profile observed with UKONIQ, ublituximab, or combinations thereof, may change as additional patients are exposed for longer durations; the risk that the combination of U2 with venetoclax will not prove to be a safe and efficacious regimen; the risk that the ULTRA-V clinical trials, if positive, will not support regulatory approval of U2 in combination with venetoclax in the U.S. or additional geographies, 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 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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