# TG Therapeutics Announces Data Presentations at the 63rd American Society of Hematology (ASH) Annual Meeting

December 13, 2021

NEW YORK, Dec. 13, 2021 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced four data presentations, including three oral presentations and one poster presentation, evaluating the combination of ublituximab, the Company's investigational anti-CD20 monoclonal antibody and UKONIQ® (umbralisib), the Company's inhibitor of PI3K-delta and CKI-epsilon, (U2), as well as U2-based triple combination therapies, including U2 plus TG's investigational BTK inhibitor TG-1701. Data presentations occurred this past weekend during the 63 rd American Society of Hematology (ASH) annual meeting and exposition. Presentation highlights are included below.

Michael S. Weiss, Chairman and Chief Executive Officer of TG Therapeutics stated, "We are excited to have showcased four presentations this past weekend, including three oral presentations, during the live ASH annual meeting. It was also gratifying to learn that two of our oral presentations, U2 in relapsed or refractory MZL and U2 as an add-on to Ibrutinib to create a time-limited therapy, were chosen for highlights of ASH. We believe these presentations further demonstrate the potential for U2 to enhance patient care and complement current standard of care for patients with B-cell malignancies."

**PRESENTATION HIGHLIGHTS**

**Oral Presentation Title: The Combination of Umbralisib Plus Ublituximab Is Active in Patients with Relapsed or Refractory Marginal Zone Lymphoma (MZL): Results from the Phase 2 Global Unity-NHL Trial**

- A total of 72 relapsed/refractory (R/R) marginal zone lymphoma (MZL) patients were enrolled in the ublituximab plus umbralisib (U2) cohort of the UNITY-NHL.
    - Patients had a median of 2 prior lines of therapy (range 1 - 9), with 25% refractory to their immediate prior therapy
- Overall Response Rate (ORR) by independent review committee (IRC) was 70%, with 21% complete response (CR) rate (n=71),
- Median duration of response (DOR) was not reached at a median follow up of 20 months.
- Grade 3/4 AEs of clinical interest included diarrhea (13%), neutropenia (18%), ALT/AST increased (15%) and non-infectious colitis (2.8%).

**Oral Presentation Title: Efficacy and Safety of Umbralisib, Ublituximab (U2), and U2 Plus Bendamustine in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL)**

- A total of 226 patients were treated within the DLBCL cohort of the UNITY-NHL trial. 30 patients received umbralisib monotherapy, 66 patients received ublituximab plus umbralisib or U2, and 130 patients received U2 plus bendamustine.
- IRC assessed response rates:
    - 43% ORR and 17% CR for U2 plus bendamustine triple combination (n=130)
    - 32% ORR and 11% CR for U2 double combination (n=66)
    - 13% ORR and 3% CR for umbralisib monotherapy (n=30)
- IRC assessed median duration of response (DOR) was 3 months for umbralisib monotherapy, 28 months for U2 combination, and 8 months for U2 plus bendamustine
- Both U2 and U2 + bendamustine demonstrated a manageable safety profile. Grade 3/4 AEs of special interest occurring in the U2 group (n=66) included ALT/AST increased (12%), non-infectious colitis (2%), diarrhea (2%), neutropenia (11%) and pneumonitis (2%). Grade 3/4 AEs of special interest occurring in the U2 plus bendamustine group (n=130) included ALT/AST increased (5%), non-infectious colitis (2%), diarrhea (7%), neutropenia (27%), pneumonitis (1%) and rash (2%).

**Oral Presentation Title: A Phase 2 Study Evaluating the Addition of Ublituximab and Umbralisib (U2) to Ibrutinib in Patients with Chronic Lymphocytic Leukemia (CLL): A Minimal Residual Disease (MRD)-Driven, Time-Limited Approach-Limited Approach**

- This study utilized an "add-on" approach, where the combination of umbralisib and ublituximab (U2) was added to therapy in patients who were on ibrutinib for greater than 6 months and had detectable minimum residual disease (MRD)
- Patients who achieve undetectable MRD (uMRD) or those who completed 24 cycles of therapy with detectable MRD stop all therapy and enter a period of treatment-free observation (TFO). Patients with clinical progression during TFO are eligible for re-treatment with the U2 + ibrutinib combination.
- 28 patients with chronic lymphocytic leukemia (CLL) were enrolled, with 27 evaluable for efficacy. Patients were on ibrutinib for a median of 21 months (range 7-67) prior to study entry.
- 77% of evaluable patients achieved uMRD, with a median time to first uMRD of 7.4 months

- Grade 3/4 AEs included diarrhea (4%), hypertension (7%), ALT/AST increased (4%) and COVID-19 (4%).

**Poster Presentation Title: The Selective Bruton Tyrosine Kinase (BTK) Inhibitor TG-1701 As Monotherapy and in Combination with Ublituximab and Umbralisib (U2) in Patients with B-Cell Malignancies**

- A total of 135 patients with R/R CLL or B-cell lymphoma were included in this presentation, with patients receiving 200 mg of TG-1701 in a dose-expansion cohort (n=61), 300 mg of TG-1701 in a CLL dose-expansion cohort (n=20), TG-1701 in combination with U2 in a dose escalation cohort (TG-1701 doses ranging from 100 – 300 mg once daily and umbralisib at either 600 mg or 800mg) (n=21), and a triple combination expansion cohort of 100mg of TG-1701 plus U2 (400 mg of umbralisib) (n=33).
- Efficacy Overall Response Rate (ORR) and Complete Response (CR) Outcomes:
    - 100% ORR observed in the CLL 300 mg QD TG-1701 monotherapy expansion cohort at a median follow up of 13.8 months (n=19)
    - 95% ORR observed in the CLL 200 mg QD TG-1701 monotherapy expansion cohort at a median follow up of 20 months (n=20)
    - 86% ORR, including 19% CR rate, observed in the 1701+U2 dose escalation cohort (using doses of 100 mg to 300 mg QD of TG-1701) at a median follow up of 20.2 months (n=21)
    - 83% ORR, including 6% CR rate, observed in the 1701+U2 dose expansion cohort (using 100 mg QD of TG-1701 and 400 mg QD of umbralisib) at a median follow up of 2.7 months (n=18)
- Grade 3/4 AEs occurring in patients treated with 200 mg QD of TG-1701 (n=61) and 300 mg QD of TG-1701 (n=20), respectively, included neutropenia (8%, 20%), ALT increased (3%, 5%), AST increased (2%, 5%) and anemia (5%, 0%). Grade 3/4 AEs occurring in patients treated with the triple combination in the U2 plus TG-1701 expansion cohort (100 mg QD TG-1701 plus 400 mg QD of umbralisib; n=19) and U2 plus TG-1701 escalation cohort (100 mg to 300 mg QD; n=21), respectively, included neutropenia (16%, 19%), ALT increased (5%, 19%), AST increased (5%, 14%).
- At the time of data cut-off, no patients had discontinued treatment due to a treatment-related adverse event across all cohorts.

The above referenced presentations are now available on the Publications page of the Company's corporate website at http://tgtxinc.com/publications.cfm.

**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.

UKONIQ® is a registered 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.

**IMPORTANT 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.

**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. In addition to the risk factors identified from time to time in our reports filed with the Securities and Exchange Commission, factors that could cause our actual results to differ materially include the following: the risk that interim, top-line, or other early clinical trial results, that may have supported the acceptance of our data for presentation or influenced our decision to proceed with additional clinical trials, will not be reproduced in final data sets or in future studies; the risk that the safety profile observed with umbralisib, ublituximab or TG-1701, or combinations thereof, may change as additional patients are exposed for longer durations; the risk that the U2 combination will not prove to be a safe and efficacious combination, or backbone for triple therapy combinations; the risk that we will not be able to meet the regulatory submission or clinical trial timelines that we project or achieve other anticipated milestones, including the risk that the evolving and unpredictable COVID-19 pandemic delays achievement of those milestones; the risk that U2 will not receive FDA approval for the treatment of CLL or, if approved, the risk that FDA will narrowly define the indication or impose certain restrictions or warnings that negatively impact the commercial potential of U2 in CLL; and the risk that further analysis of data from the UNITY-CLL study will lead the Company to voluntarily withdraw its currently pending U.S. regulatory applications for U2. 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, 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.

**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