TG Therapeutics Announces Data from the UNITY-CLL Phase 3 Trial Presented at the 63rd American Society of Hematology (ASH) Annual Meeting

December 14, 2021

NEW YORK, Dec. 14, 2021 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced two data presentations, highlighted data from the UNITY-CLL Phase 3 trial evaluating the combination of ublituximab, the Company's investigational anti-CD20 monoclonal antibody and UKONIQ (umbralisib), the Company's inhibitor of PI3K-delta and CK1-epsilon, (U2), in patients with both treatment naïve and relapsed or refractory chronic lymphocytic leukemia (CLL). Data presentations occurred yesterday evening during the 63rd 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 pleased to share two presentations last night at the ASH annual meeting which included additional analyses of the UNITY-CLL Phase 3 trial evaluating the U2 combination in patients with both treatment naïve and relapsed or refractory CLL. We believe these presentations showcase the versatility of the U2 combination both by treatment subgroup, and also interestingly in a patient population generally characterized as unsuitable for BTKi-based therapy. While significant advances have been made in the treatment of CLL, there still remains underserved patients who may not be good candidates for or fail to respond to currently available treatments."

PRESENTATION HIGHLIGHTS

Poster Presentation Title: Efficacy and Safety of Ublituximab in Combination with Umbralisib (U2) in Patients with Chronic Lymphocytic Leukemia (CLL) By Treatment Status: A Sub-Analysis of the Phase 3 Unity-CLL Study

- A total of 210 CLL patients were enrolled in the U2 cohort of the UNITY-CLL trial, including 119 treatment naïve and 91 previously treated.
- Efficacy and safety highlights for the treatment naïve (TN) population included:
  - Independent review committee (IRC) assessed progression-free survival (PFS) of U2 in the TN population was 38.5 months, with two-year PFS of 76.6%
  - 84% IRC-assessed overall response rate (ORR) in the TN population, including 5% complete response (CR)/complete response with incomplete marrow recovery (CRi)
  - Responses were durable with 76% maintaining response at 2 years
  - Grade 3/4 adverse events (AEs) of special interest occurring in the TN population included ALT elevation (12%), AST elevation (8%), rash (3%), pneumonia (7%), non-infectious colitis (3%), pneumonitis (1%) and opportunistic infections (1%).
- Efficacy and safety highlights for the previously treated population (PT) included:
  - IRC-assessed PFS in the PT population was 19.5 months, with two-year PFS of 41.3%
  - 82% IRC-assessed ORR in the PT population, including 4% CR/CRi
  - Responses were durable, with 43% maintaining response at 2 years
  - Grade 3/4 adverse events (AEs) of special interest occurring in the PT population included ALT elevation (3%), AST elevation (2%), rash (1%), pneumonia (11%) and opportunistic infections (1%).

Poster Presentation Title: Favorable Outcomes for Patients Treated with U2 with Co-Morbidities or Concomitant Medications: A Retrospective Analysis of Unity-CLL Phase 3 Trial

- A total of 210 CLL patients were enrolled in the U2 cohort of the UNITY-CLL trial, including 119 treatment naïve and 91 previously treated.
- 131 (64%) of U2 treated patients had at least 1 comorbid condition or concomitant medication (conmed) that could pose potential issues with BTKi therapy.
- 88% ORR, including 5% CR, for those patients with at least 1 comorbidity or conmed (n=131), compared to 83% ORR, including 5% CR, for the entire U2 population (n=210).
- No difference in IRC-assessed PFS was observed between the group of patients with at least 1 comorbidity or conmed compared to the entire U2 population (31.9 months for both groups).
- Grade 3/4s AEs of clinical interest in the group of patients with at least 1 comorbidity or conmed and the entire U2 population respectively, included ALT elevation (8%, 8%), AST elevation (4%, 5%), non-infectious colitis (3%, 2%) and pneumonitis (1%, 0.5%).

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.

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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 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 regulatory 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.

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