TG Therapeutics Announces Combination Data Presentations at the XIX International Workshop on Chronic Lymphocytic Leukemia (iwCLL)

September 20, 2021

Investor & Analyst Virtual Event to Discuss Phase 1 U2 + Venetoclax Data to be held today, September 20, 2021 at 8:30 AM ET

NEW YORK, Sept. 20, 2021 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX), today announced data presentations at the XIX International Workshop on Chronic Lymphocytic Leukemia (iwCLL). Data highlights from each presentation are included below.

The Company will also host a virtual investor and analyst event today, September 20, 2021 at 8:30 AM ET, to review the updated Phase 1 data evaluating the investigational combination of UKONIQ® (umbralisib) and ublituximab (U2) plus venetoclax presented at iwCLL, as well as provide an overview of the ULTRA-V Phase 2/3 trial.

Michael S. Weiss, the Company's Chairman and Chief Executive Officer, stated, “The iwCLL conference this past weekend was an exciting meeting, where we were able to share data from four combination trials, including updated data from our Phase 1/2 study of U2 plus venetoclax. Our goal has been to develop combination therapies utilizing U2 as a backbone and we believe the data presented this weekend showcase the breadth of the program, which includes combinations with targeted therapy as well as immunotherapy. With a March 25, 2022 PDUFA date in the US, we are excited about the potential approval of the U2 regimen for CLL patients and hope you all can join us this morning for our virtual event to review some of the encouraging data presented this past weekend.”

IwCLL 2021 DATA HIGHLIGHTS

Oral Presentation Title: Umbralisib Plus Ublituximab (U2) Is Superior to Obinutuzumab Plus Chlorambucil (O+Chl) in Patients with Treatment-Naïve (TN) and Relapsed/Refractory (R/R) Chronic Lymphocytic Leukemia (CLL): Results from the Phase 3 UNITY-CLL Study

- 421 patients were randomized to the U2 (n=210) or O+Chl (n=211) arms; 57% of patients were treatment-naïve and 43% had relapsed/refractory (R/R) CLL
- At a median follow-up of 36.7 months, U2 significantly prolonged independent review committee (IRC) assessed progression-free survival (PFS) vs O+Chl (median 31.9 months vs 17.9 months; hazard ratio 0.546 (p<0.0001))
- PFS improvement with U2 vs O+Chl was consistent across all subgroups examined including treatment naïve patients (median 38.5 months vs 26.1 months, hazard ratio 0.482) and relapsed/refractory patients (median 19.5 months vs 12.9 months, hazard ratio 0.601)
- Overall response rate (ORR) was significantly higher with U2 compared to O+Chl (83.3% vs 68.7%; p<0.001)
- For the U2 arm, at a median treatment exposure of 21 months, most adverse events (AEs) were Grade 1 or 2 in severity and were relatively balanced between the treatment naïve and previously treated populations
- Grade 3/4 Adverse Events (AEs) of clinical interest (U2 vs O+Chl) included elevated ALT (8.3% vs 1.0%), elevated AST (5.3% vs 2.0%), non-infectious colitis (1.9% vs 0%), infectious colitis (0.5% vs 0.5%), pneumonitis (0.5% vs 0%), rash (2.4% vs 0.5%), and opportunistic infections (5.8% vs. 1.5%)

Oral Presentation Title: A Phase 1/2 Study of Umbralisib, Ublituximab, and Venetoclax in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL)

- Regimen was administered with 3 cycles of U2 as induction in cycles 1 through 3, U2 plus venetoclax in cycles 4, 5 and 6, followed by umbralisib plus venetoclax in cycles 7 through 12 in patients with relapsed or refractory (R/R) CLL. Patients with centrally confirmed undetectable minimal residual disease (uMRD) in the bone marrow after cycle 12 were permitted to stop all therapy, while MRD detectable patients continued on single agent umbralisib.
- 47 patients have now been treated as of the data cutoff with 57% of patients previously exposed to a BTK inhibitor
- Best Overall Response Rate (ORR) was 100% amongst evaluable patients (n=46), including 37% complete response (CR) rate
- At cycle 12, 91% of patients (n=34) achieved undetectable minimal residual disease (uMRD) in the peripheral blood (PB), and 72% of patients (n=32) achieved uMRD in the bone marrow (BM)
- At a median follow up of 24.5 months, median progression-free survival has not been reached
- Grade 3/4 adverse events (AEs) occurring in >5% of patients were neutropenia (28%), leukopenia (15%), lymphocytopenia (15%), infusion related reactions (9%), diarrhea (9%), and anemia (6%). No TLS events were observed during venetoclax administration

Oral Poster Presentation Title: TG-1701, a Selective Bruton Tyrosine Kinase (BTK) Inhibitor, as Monotherapy and in Combination with Ublituximab and Umbralisib (U2) in Patients with Chronic Lymphocytic Leukemia

- A total of 50 patients with R/R CLL have been treated with TG-1701, with patients receiving monotherapy in the dose-escalation cohort (n=6), 200 mg in a dose-expansion cohort (n=20), 300 mg in a dose-expansion cohort (n=20), or TG-1701 in combination with U2 in the dose escalation cohort (n=4).
- TG-1701 monotherapy was well tolerated and the maximum tolerated dose was not reached up to 400 mg QD.
- Grade 3/4 AEs occurring in patients treated with 200 mg QD of TG-1701 (n=20), included neutropenia (10%), anemia (5%) and arthralgia (5%). Grade 3/4 AEs occurring in patients treated with 300 md QD of TG-1701 (n=20), included neutropenia (20%), COVID-19 (5%), ALT increased (5%) and AST increased (5%).
- 100% ORR observed in the 300 mg QD monotherapy expansion cohort at a median follow up of 12 months (n=19)
- 95% ORR observed in the 200 mg QD monotherapy expansion cohort at a median follow up of 19 months (n=20)
- 100% ORR observed in the 1701+U2 dose escalation (using doses of 100 mg to 300 mg QD of TG-1701) at a median follow up of 19 months (n=3)

Poster Presentation Title: Phase I/II Study of Umbralisib (TGR-1202), Ublituximab (TG-1101), and Pembrolizumab in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia and Richter's Transformation: 5-Year Follow-up

- A total of 20 patients with R/R CLL or Richter's Transformation (RT) were treated with the triple combination of ublituximab, umbralisib, and pembrolizumab. Patients with CLL received 2 cycles of the U2 regimen before pembrolizumab was added for an additional 4 cycles, followed by umbralisib maintenance. Patients with RT received U2 + pembrolizumab for the first 4 cycles, followed by U2 maintenance. Twenty patients were evaluable for safety (11 CLL patients and 9 RT patients) and 19 were evaluable for efficacy (11 CLL and 8 RT).
- The triple combination was well tolerated, with immune mediated toxicities not appearing above what would be expected with either umbralisib or pembrolizumab alone. Grade 3/4 AEs occurring in >20% of patients (n=20) include, neutropenia (45%), thrombocytopenia (15%), ALT increase (15%), leukopenia (10%), nausea (5%), fatigue (5%), and anemia (5%).
- In this heavily pre-treated cohort with a median of 2 (1-9) prior lines of therapy:
  -- 91% ORR in patients with R/R CLL (n=11)
  -- 83% ORR in BTK refractory CLL patients (n=6), with 4 of 5 responders achieving a response to U2 alone at the patient's first efficacy assessment, prior to the addition of pembrolizumab
  -- 25% ORR in patients with RT (n=8), including 25% CR rate

The above data presentations are available on the Publications page, located within the Pipeline section, of the Company's website at www.tgtherapeutics.com/publications.cfm.

INVESTOR & ANALYST VIRTUAL EVENT INFORMATION

The Company will host a virtual event today, September 20, 2021 at 8:30 AM ET, to discuss the updated Phase 1 data evaluating UKONIQ® (umbralisib) and ublituximab (U2) in combination with venetoclax in patients with CLL as well as provide an overview of the Phase 2/3 ULTRA-V program.

To attend the live event, please visit the Events page, located within the Investors & Media section, of the Company's website at http://ir.tgtherapeutics.com/events. Following the live event, an archive file will be available for replay, for a period of 30 days after the call.

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 UKONIQ and ublituximab (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 overall response rate (ORR), including complete response (CR) rate, progression-free survival (PFS), and undetectable minimal residual disease (uMRD) rate after 12 cycles of therapy. The trial enrolled approximately 50 CLL patients and is being led by Dr. Paul Barr of the Wilmot Cancer Institute, University of Rochester Medical Center.

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 UKONIQ and ublituximab (U2) 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 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 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 109/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. Such forward-looking statements include but are not limited to statements regarding our clinical programs, including our clinical trials evaluating the investigational combination of UKONIQ® (umbralisib) and ublituximab (U2) plus venetoclax.

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 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, including with venetoclax and TG-1701; the risk that the clinical development of our products and regimens will take longer and/or cost more than planned; the uncertainties inherent in research and development; the risk that the clinical results from our registrational trials will not support regulatory approval of our investigational products or regimens, including the risk that FDA will not approve ublituximab in combination with umbralisib for the treatment of CLL; the risk that if approved, our products will not be commercially successful; 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 SEC.

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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