TG Therapeutics Announces Publication of Results from the UNITY-NHL Phase 2b Trial Evaluating Umbralisib Monotherapy in Patients with Relapsed or Refractory Indolent non-Hodgkin Lymphoma in the Journal of Clinical Oncology

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NEW YORK, March 09, 2021 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX) today announced the publication of results from the UNITY-NHL Phase 2b trial evaluating UKONIQ™ (umbralisib), the Company's inhibitor of PI3k-delta and CK1-epsilon, in patients with relapsed or refractory indolent non-Hodgkin Lymphoma (NHL) in the Journal of Clinical Oncology (JCO).

Michael S. Weiss, the Company's Executive Chairman and Chief Executive Officer stated, "We are extremely pleased that the results of the UNITY-NHL trial which supported the recent approval of umbralisib, now called UKONIQ, in relapsed or refractory marginal zone and follicular lymphoma, have been published in the prestigious Journal of Clinical Oncology. The data published yesterday, and previously presented at the ASH 2020 conference, highlight the utility of UKONIQ across these diseases. As the first and only inhibitor of both PI3K-delta and CK1-epsilon, which is now commercially available, we believe UKONIQ offers an important new treatment option for patients."

Pier Luigi Zinzani, MD, PhD, Professor, Institute of Hematology, "L. e A. Seràgnoli", University of Bologna, and Global Chair of the UNITY-NHL Phase 2b study stated, "The data published yesterday as well as the recent U.S. FDA approval of umbralisib in relapsed or refractory marginal zone lymphoma and follicular lymphoma, are encouraging for patients suffering from these diseases, especially given the lack of a standard of care in these settings. As we see from the UNITY-NHL publication, umbralisib offers meaningful clinical activity across both marginal zone and follicular lymphoma and a manageable safety profile with relatively low rates of immune mediated toxicities and discontinuations due to adverse events."

The manuscript includes data from 208 patients with relapsed or refractory iNHL, including 69 marginal zone lymphoma (MZL), 117 follicular lymphoma (FL), and 22 small lymphocytic lymphoma (SLL) patients who were unresponsive to prior treatments (≥1 MZL; ≥2 FL/SLL), including anti-CD20–based therapy. Patients were administered umbralisib 800 mg orally once-daily until disease progression, unacceptable toxicity, or study withdrawal. The primary end point was overall-response-rate (ORR) as assessed by an independent review committee (IRC) based on the Lugano classification.

Key highlights from this manuscript include:

- The ORR was 47.1% across all relapsed or refractory iNHL patients treated (n=208)
- At a median follow-up of 27.8 months patients with relapsed or refractory MZL demonstrated:
  - 49.3% ORR with 16% Complete response (CR) rate (IRC assessed)
  - Median duration of response (DOR) was not reached (95% CI, 10.3 – not estimable) and
  - Median Progression Free Survival (PFS) was not reached (95% CI, 12.1 – not estimable)
- At a median follow-up of 27.5 months patients with relapsed or refractory FL demonstrated:
  - 45.3% ORR with 5.1% achieving a CR (IRC assessed)
  - Median DOR of 11.1 months (95% CI, 8.3–15.6)
  - Median PFS was 10.6 months
- Grade ≥3 treatment emergent adverse events (TEAEs) reported in ≥10% of patients included: neutropenia (11.5%) and diarrhea (10.1%). Increased ALT/AST (grade ≥3) occurred in 6.7%/7.2% of patients.
- Other AEs of special interest included pneumonitis (1.4%; grade ≥3 1.0%) and non-infectious colitis (1.9%; grade >3 0.5%).
- A total of 31 patients (14.9%) discontinued due to a treatment-related adverse event.

These data are described further in the manuscript entitled, "Umbralisib, a Dual PI3Kδ/CK1ε Inhibitor in Patients with Relapsed/Refractory Indolent Lymphoma," which was published online yesterday in the Journal of Clinical Oncology. The online version of the article can be accessed at https://ascopubs.org/doi/full/10.1200/JCO.20.03433.

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.

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.

Such forward looking statements include but are not limited to statements regarding expectations for the commercial launch and availability of UKONIQ™ (umbralisib) for relapsed or refractory (R/R) marginal zone lymphoma (MZL) and follicular lymphoma (FL); anticipated healthcare professional and patient acceptance and use of UKONIQ for the FDA-approved indications; and perceptions of the UNITY-NHL data.

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 Company's ability to establish and maintain a commercial infrastructure, and to successfully launch, market and sell UKONIQ or future products, if approved; failure to obtain and maintain requisite regulatory approvals, including the risk that the Company fails to satisfy post-approval regulatory requirements, such as the submission of sufficient data from a confirmatory clinical study; the risk that as UKONIQ or any future approved products are used more widely or for a longer duration after being brought to market, data may emerge from clinical studies, including confirmatory or other post-marketing studies, or from adverse event reporting that may affect the perceived profile and commercial potential of our products; the potential for variation from the Company's projections and estimates about the potential market for UKONIQ or the Company's product candidates due to a number of factors, including for example, limitations that regulators may impose on the required labeling for the proposed treatment population for UKONIQ or our other product candidates; the Company's ability to meet post-approval compliance obligations (on topics including but not limited to product quality, product distribution and supply chain, pharmacovigilance, and sales and marketing); potential regulatory challenges to the Company's plans to seek expanded or additional indications for UKONIQ in the U.S. or plans to seek marketing approval for the product in additional geographies, outside of the U.S.; the Company's reliance on third parties for manufacturing, distribution and supply, and a range of other support functions for our clinical and commercial products, including UKONIQ; 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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