TG Therapeutics Announces Publication of Results from an Integrated Safety Analysis of UKONIQ® (umbralisib) in Blood Advances

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NEW YORK, Sept. 23, 2021 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ: TGTX) today announced the publication of results from an integrated safety analysis of UKONIQ® (umbralisib), the Company's inhibitor of PI3k-delta and CK1-epsilon, in patients with relapsed or refractory lymphoid malignancies in *Blood Advances*, a journal of the American Society of Hematology.

Michael S. Weiss, the Company's Chairman and Chief Executive Officer stated, "We are pleased that the integrated safety analysis of 371 patients treated with UKONIQ has been published in *Blood* Advances. We believe these data further support the differentiated safety profile of UKONIQ, the first and only PI3k-delta and CK1-epsilon inhibitor, which is now commercially available to patients with relapsed or refractory marginal zone lymphoma and follicular lymphoma. As we strive toward obtaining FDA approval of the investigational combination of UKONIQ and ublituximab, U2, in CLL by the PDUFA goal date of March 25, 2022, furthering our understanding of the safety and tolerability profile of UKONIQ remains paramount to us."

Matthew S. Davids, MD, MMSc, lead author of the integrated safety study and Director of Clinical Research in the Division of Lymphoma at Dana-Farber Cancer Institute stated, "Historically, the use of PI3K-delta inhibitors has been limited by high discontinuation rates. The integrated safety data analysis of umbralisib published [today/yesterday] is encouraging for patients, especially given the low rate of discontinuations due to adverse events observed. Our analysis further underscores the potential role of umbralisib in the treatment of relapsed or refractory marginal zone and follicular lymphoma and may support the future utilization of umbralisib in combination therapies for patients with lymphoid malignancies."

The manuscript includes integrated comprehensive toxicity data from 4 open-label phase 1 and 2 studies that included 371 adult patients with relapsed or refractory non-Hodgkin lymphoma (NHL), including patients with follicular lymphoma (n=147), marginal zone lymphoma (n=81), diffuse large B-cell lymphoma/mantle cell lymphoma (n=74), chronic lymphocytic leukemia (n=43) and other (n=25). All patients were treated with umbralisib at 800mg or higher once daily. At data cutoff, median duration of umbralisib treatment was 5.9 months (range, 0.1-75.1), and 107 patients (28.8%) received umbralisib for ≥12 months.

Key highlights from this manuscript include:

- The most common grade ≥3 treatment-emergent adverse events (TEAEs) were neutropenia (11.3%), diarrhea (7.3%), and increase aminotransferases (5.7%).
- AEs of special interest were limited and included pneumonia in 29 patients (7.8%), noninfectious colitis in 9 patients (2.4%), and pneumonitis in 4 patients (1.1%).
- Treatment-emergent serious AEs occurred in 95/371 patients (25.6%).
- AEs led to discontinuation of umbralisib in 51 patients (13.7%).
- No cumulative toxicity over time was observed.

These data are described further in the manuscript entitled, "Integrated safety analysis of umbralisib, a dual PI3Kδ/CK1ε inhibitor, in relapsed/refractory lymphoid malignancies," which was published online in *Blood Advances*. The online version of the article can be accessed at https://pubmed.ncbi.nlm.nih.gov/34547767/.

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.

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 UKONIQ® (umbralisib) for the treatment of relapsed or refractory (R/R) marginal zone lymphoma (MZL) and follicular lymphoma (FL); the safety and tolerability profile of UKONIQ; and ongoing research of combination regimens that include UKONIQ. 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 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 safety and tolerability profile and commercial potential of our products; the Company's ability to maintain a commercial infrastructure and to successfully market and sell UKONIQ or future products, if approved; approval of expanded or additional indications for UKONIQ and for our product candidates, including ublituximab, in the U.S.or to our ability to obtain marketing approval for any of our products in additional geographies, outside of the U.S.; 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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