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TG Therapeutics, Inc. Announces Publication in *Blood* Describing a Novel Complimentary Mechanism of the PI3K-delta Inhibitor, TGR-1202

Complimentary inhibition of PI3K-delta and casein kinase-1 (CK1) epsilon by TGR-1202 may provide mechanistic rationale for clinical activity in aggressive c-Myc driven lymphomas

Publication outlines strong rationale for combining TGR-1202 and carfilzomib in the recently announced combination study in both indolent and aggressive lymphomas

NEW YORK, Oct. 27, 2016 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ:TGTX) announced the publication of preclinical data describing the synergy of the Company's next generation, once daily, PI3K-delta inhibitor, TGR-1202, with the proteasome inhibitor carfilzomib and the unique effects of the combination to silence c-Myc in various preclinical lymphoma and myeloma models. In addition, the manuscript also, for the first time, reports on TGR-1202's unique complimentary mechanism of inhibiting the protein kinase casein kinase-1 (CK1) epsilon, which may contribute to the silencing of c-Myc and explain TGR-1202's clinical activity in aggressive lymphoma, including Diffuse Large B-cell Lymphoma (DLBCL). The preclinical data are described further in the manuscript titled, "Silencing c-Myc Translation as a Therapeutic Strategy through Targeting PI3K Delta and CK1 Epsilon in Hematological Malignancies," which was published online yesterday in the First Edition section of *Blood*, the Journal of the American Society of Hematology. The online version of the article can be accessed at www.bloodjournal.org.

"We want to thank Dr. Deng, Dr. O'Connor, and the team from Columbia Presbyterian Medical Center and the Center for Lymphoid Malignancies for their exhaustive and comprehensive interrogation of TGR-1202 and the elucidation of this novel complimentary mechanism. For quite some time we have been presenting the differentiated safety profile observed with TGR-1202 and the differentiated chemical structure compared to other PI3K-delta inhibitors. This preclinical work demonstrates that TGR-1202 not only potently targets PI3K-delta but in addition uniquely targets a relatively novel kinase, CK1-epsilon, which perhaps offers another rationale for the differentiated activity and safety effects we have seen in patients. We look forward to exploring this exciting concept further in the recently launched clinical trial," stated Michael S. Weiss, the Company's Executive Chairman and Interim Chief Executive Officer.

"The data in this paper clearly demonstrates that TGR-1202 and carfilzomib in combination is markedly synergistic and selectively silenced c-Myc compared to combinations with idelalisib and bortezomib. In addition, we were excited to identify and elucidate the previously unknown mechanism of TGR-1202 and its effect on CK1 epsilon which was not exhibited by either idelalisib or duvelisib based on a kinome profiling platform analyzed. We believe this research may help explain in part the preliminary activity demonstrated by TGR-1202 in DLBCL. Given TGR-1202's distinct safety profile as a single agent and its uniquely demonstrated ability to be used in combination with other agents, we look forward to bringing this novel combination to the clinic in our recently announced Phase 1 study of TGR-1202 and carfilzomib in patients with lymphoma," stated Dr. Owen A. O'Connor, Professor of Medicine and Experimental Therapeutics, Director Lymphoid Malignancies at Columbia Presbyterian Medical Center.

Based on this extensive preclinical work, the Company recently announced the launch of a Phase 1/2 study to evaluate the safety and efficacy of TGR-1202 in combination with carfilzomib, in patients with relapsed or refractory lymphoma, particularly c-Myc driven lymphomas which are aggressive in nature. This study is currently open to enrollment at the Center for Lymphoid Malignancies, Columbia Presbyterian Medical Center, New York, NY. More information on this clinical study can be found at www.clinicaltrials.gov.

ABOUT TG THERAPEUTICS, INC.

TG Therapeutics is a biopharmaceutical company focused on the acquisition, development and commercialization of novel treatments for B-cell malignancies and autoimmune diseases. Currently, the company is developing two therapies targeting hematological malignancies and autoimmune diseases. TG-1101 (ublrituximab) is a novel, glycoengineered monoclonal antibody that targets a specific and unique epitope on the CD20 antigen found on mature B-lymphocytes. TG Therapeutics is also developing TGR-1202, an orally available PI3K delta inhibitor. The delta isoform of PI3K is strongly expressed in cells of hematopoietic origin and is believed to be important in the proliferation and survival of B-lymphocytes. Both TG-1101 and TGR-1202 are in clinical development for patients with hematologic malignancies, with TG-1101 recently entering clinical development for autoimmune disorders. The Company also has preclinical programs to develop IRAK4 inhibitors, BET

inhibitors, and anti-PD-L1 and anti-GITR antibodies. TG Therapeutics is headquartered in New York City.

Cautionary Statement

Some of the statements included in this press release, particularly those with respect to current or future clinical trials, the timing of commencing or completing such trials and business prospects for TG-1101, TGR-1202, the IRAK4 inhibitor program, the BET inhibitor program, and the anti-PD-L1 and anti-GITR antibodies may be 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. Among the factors that could cause our actual results to differ materially are the following: our ability to successfully and cost-effectively complete preclinical and clinical trials for TG-1101, TGR-1202, the IRAK4 inhibitor program, the BET inhibitor program, and the anti-PD-L1 and anti-GITR antibodies; the risk that early preclinical and clinical results that supported our decision to move forward with TG-1101, TGR-1202, the IRAK4 inhibitor program, the BET inhibitor program, and the anti-PD-L1 and anti-GITR antibodies or combination trials which include any of the aforementioned product candidates will not be reproduced in additional patients or in future studies; the risk that trends observed which underlie certain assumptions of future performance of TGR-1202 will not continue, the risk that TGR-1202 will not produce satisfactory safety and efficacy results to warrant further development following the completion of the current Phase 1 study; the risk that the combination of TG-1101 and TGR-1202, referred to as TG-1303, will not prove to be a safe and efficacious backbone for triple and quad combination therapies; the risk that the data (both safety and efficacy) from future clinical trials will not coincide with the data produced from prior preclinical and clinical trials; the risk that trials will take longer to enroll than expected; our ability to achieve the milestones we project over the next year; our ability to manage our cash in line with our projections, and other risk factors identified from time to time in our reports filed with the 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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