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TG Therapeutics, Inc. Recaps Positive Data from the Phase 3 GENUINE Trial and Data from the Triple Combination of TG-1101, TGR-1202, and Ibrutinib at the 14th International Conference on Malignant Lymphoma

GENUINE Phase 3 trial met its primary endpoint with TG-1101 (ublituximab) plus ibrutinib increasing Overall Response Rate (ORR) by > 70% over ibrutinib alone in patients with high-risk CLL

Triple combination of TG-1101, TGR-1202 and ibrutinib produced 100% ORR (19 of 19) in patients with CLL/SLL, including 32% CR rate, with a favorable safety profile observed

NEW YORK, June 16, 2017 (GLOBE NEWSWIRE) -- TG Therapeutics, Inc. (NASDAQ:TGTX), today recapped clinical data from its Phase 3 GENUINE trial of TG-1101 (ublituximab), the Company's novel glycoengineered anti-CD20 monoclonal antibody in combination with ibrutinib, the BTK inhibitor, as well as data from the chemo-free triple combination of TGR-1202 (umbralisib), the Company's oral, next generation PI3K delta inhibitor, TG-1101, and ibrutinib. Data from these trials were presented today during oral sessions at the 14th International Conference on Malignant Lymphoma (ICML) in Lugano, Switzerland. These data sets were presented previously at the American Society of Clinical Oncology (ASCO) annual meeting earlier this month. Highlights from each of these data sets are included below.

Michael S. Weiss, the Company's Executive Chairman and Chief Executive Officer stated, "CLL patients with high-risk cytogenetics continue to represent a challenge and continue to progress more rapidly on ibrutinib than other patients. Improving ibrutinib therapy for these hard to treat patients still represents an unmet medical need. We are pleased to be the first Company to demonstrate in a randomized Phase 3 trial an approach to potentially improve outcomes for those patients. As presented today at ICML, and last week at ASCO, the GENUINE Phase 3 trial showed that by adding TG-1101 to ibrutinib, we could improve overall response rate, CR rate, and MRD negativity in high risk patients. We believe the data provide a compelling case for accelerated approval given the demonstrated clinical benefit with limited additional safety risk, and we look forward to sharing these data formally with the FDA later this year." Mr. Weiss continued, "Additionally, at ICML today, and last week at ASCO, we had an opportunity to present data on a triple therapy where we layered our proprietary PI3K-delta inhibitor, TGR-1202, to the TG-1101 plus ibrutinib combination, and demonstrated even further enhanced activity, with 100% ORR by iwCLL criteria and a high level of complete responses. These data further confirm our approach of building toward multi-drug regimens to enhance the outcome for patients, ideally achieving CRs and avoiding lifelong therapy. We look forward to continuing to explore unique combinations, with TG-1101 (ublituximab) plus TGR-1202 (umbralisib) or 'U2' as the backbone."

Highlights from today's presentations include the following:

Oral Presentation: Ublituximab and ibrutinib for previously treated genetically high-risk chronic lymphocytic leukemia: Results of the GENUINE Phase 3 study (Abstract #101)

This presentation includes data from the GENUINE Phase 3 trial, a multicenter, randomized trial (NCT02301156), which assessed the efficacy and safety of TG-1101 plus ibrutinib versus ibrutinib alone in patients with high-risk CLL. For the trial, high-risk was defined as having any one or more of the following centrally confirmed features: 17p deletion, 11q deletion, or p53 mutation. The GENUINE study was designed to demonstrate the value of adding TG-1101, a potent next generation glycoengineered anti-CD20 monoclonal antibody to ibrutinib monotherapy in high risk CLL, and was powered to show a statistically significant improvement in ORR of 30%, with a minimal absolute detectable difference between the two arms of approximately 20%.

The trial met its primary endpoint, demonstrating a statistically significant improvement in Overall Response Rate (ORR), as assessed by blinded independent central radiology and hematology review by iwCLL (Hallek 2008) criteria, compared to ibrutinib alone in both the Intent to Treat (ITT) population ($p=0.001$) and Treated population ($p < 0.001$). Per iwCLL guidelines, all responders required confirmation of response for a minimum duration of 2 months. The ITT population includes all 126 randomized patients (64 in the TG-1101 plus ibrutinib arm and 62 in the ibrutinib alone arm) while the Treated population includes all ITT patients that received at least one dose of either study drug (59 in the TG-1101 plus ibrutinib arm and 58 in the ibrutinib alone arm).

Patient Demographics

One hundred and twenty-six (126) patients were randomized on the GENUINE Phase 3 Trial. 100% of patients were high risk and had either 17p deletion, 11q deletion or p53 mutation. Sixty-four percent (64%) of patients in the TG-1101 plus ibrutinib arm and 66% of patients in the ibrutinib alone arm had 17p deletion and/or a p53 mutation while 36% and 34% of patients in the TG-1101 plus ibrutinib and ibrutinib alone arms, respectively, had an 11q deletion only. The median age of patients on either arm was 67 years and the median number of prior lines of therapy for either arm was 3.

Safety & Tolerability

One hundred and seventeen (117) patients were evaluable for safety (59 patients in the TG-1101 plus ibrutinib arm, and 58 patients in the ibrutinib alone arm). The combination was well tolerated and, apart from infusion related reactions, the addition of TG-1101 did not appear to alter the safety profile of ibrutinib monotherapy. Neutropenia, occurring in 9% of patients, was the most commonly reported Grade 3/4 Adverse Event (AE) in the combination arm, followed by infusion related reactions and anemia, each reported in 5% of patients. Notably, the majority of infusion related reactions (IRR) were Grade 1 or 2 in severity, with only 5% Grade 3/4 IRR observed. Median follow-up for this study was approximately 11.4 months.

Clinical Activity

Response Rates

	TG-1101 plus ibrutinib	ibrutinib	P-value
Treated Population (n)	n=59	n=58	
Overall Response Rate (ORR)	78%	45%	P < 0.001
Complete Response (CR)	7%	0%	NS
MRD-Negative	19% *(n=53)* *	2% *(n=53)* *	P < 0.01

**Patients evaluable for MRD included those enrolled > 4 months prior to data cutoff date of February 15, 2017. MRD analyzed by central lab, 7-color flow cytometry*

In addition to the improvements in ORR, CR, and MRD-negativity, a trend in improvement of Progression-Free Survival (PFS) in the combination arm of TG-1101 plus ibrutinib as compared to ibrutinib alone, however it was not statistically significant at the time of the analysis.

ABOUT THE PHASE 3 GENUINE STUDY

The Phase 3 GENUINE study is a randomized, open label, multicenter clinical trial to evaluate the safety and efficacy of TG-1101 (ublituximab) plus ibrutinib compared to ibrutinib alone in adult patients with high risk Chronic Lymphocytic Leukemia (CLL) who received at least one prior therapy for their disease.

The study was conducted at 160 clinical trial sites in the US and Israel and randomized 126 patients. Patients received ibrutinib orally at 420 mg once daily in both arms and in the treatment arm those patients also received intravenous infusions of TG-1101 at 900 mg dosed on days 1, 8 and 15 of cycle 1 and day 1 of cycles 2-6. Patients in the treatment arm who had not progressed received quarterly infusions of TG-1101 maintenance at 900 mg.

Oral Presentation: Chemo-free triplet combination of TGR-1202, ublituximab, and ibrutinib is well tolerated and highly active in patients with advanced CLL and NHL (Abstract #102)

This oral presentation includes data from patients with Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) and Non-Hodgkin's Lymphoma (NHL) treated with the triple combination of TGR-1202, TG-1101 and ibrutinib. All patients were relapsed or refractory to prior therapy, except 3 CLL patients who were treatment naïve. Three cohorts for each CLL/SLL and NHL were evaluated with TGR-1202 dose escalation starting with doses of 400 mg (cohort 1), followed by 600 mg (cohort 2) and 800 mg (cohort 3), in combination with TG-1101 at 900 mg and ibrutinib daily at 420 mg (CLL) and 560 mg (NHL).

Safety & Tolerability

Thirty-eight (38) patients were evaluable for safety (20 CLL/SLL patients, and 18 NHL patients). The triple combination appeared to be well tolerated in all patients, with neutropenia (32% all grades, 18% Grade 3/4) and pneumonia (18% all grades, 11% Grade 3/4), being the only Grade 3/4 AEs in > 10% of patients. Of the 38 patients treated to date, only two AEs (sepsis and pneumonia) led to treatment discontinuation. Median time on study was 11.1 months (range 0.4 - 30+ months) with 81% of patients on study > 6 months.

Clinical Activity
Clinical activity was observed at all dose levels with 36 of 38 patients evaluable for efficacy (19 CLL/SLL patients, and 17 NHL patients), with 2 patients having discontinued prior to first efficacy assessment (1 pneumonia, and 1 investigator discretion).

CLL/SLL Efficacy highlights include:

- 100% (19 of 19) Overall Response Rate (ORR), including a 32% Complete Response (CR) rate observed in patients with CLL/SLL (4 of 6 CR's pending bone marrow confirmation)
- 50% of the CLL patients had a 17p and/or 11q deletion
- 3 CLL patients had prior BTK and/or PI3Kδ inhibitor therapy, including one patient refractory to both idelalisib and ibrutinib who attained a complete response (ongoing for 1.5+ years)

NHL Efficacy highlights include:

- Response Rates observed in patients with NHL:
  - 100% (2 of 2) ORR, including one CR in patients with Marginal Zone Lymphoma (MZL)
  - 100% (4 of 4) ORR, including 50% CR rate in patients with Mantle Cell Lymphoma (MCL)
  - 80% (4 of 5) ORR, including 20% CR rate in patients with Follicular Lymphoma (FL)
  - 17% (1 of 6) ORR in patients with Diffuse Large B-cell Lymphoma (DLBCL)
- FL patients were heavily pretreated including 2 with prior Autologous Stem Cell Transplant (ASCT), 1 refractory to prior ibrutinib, and 1 with 5 prior lines of rituximab based therapy
- DLBCL patients had a median of 4 prior therapies, and 4 of 6 were of non-GCB subtype

PRESENTATION DETAILS:

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

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 (ublituximab) 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 (umbralisib), 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 also in clinical development for autoimmune disorders. The Company also has pre-clinical 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 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. 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 are the following: the risk that 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 future studies; the risk that the combination of TG-1101 and TGR-1202, referred to as TG-1303 and being studied in the chemo-free triple combination of TG-1101 plus TGR-1202 plus ibrutinib and in the UNITY clinical trials and other combination trials, will not prove to be safe and efficacious for any indication or as a backbone for current or future triple and/or quad therapies; the risk that even if the company is successful in developing its drugs through FDA approval and on to the market, that the cost efficiencies anticipated through proprietary combinations may not be realized in the marketplace. 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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