

TG THERAPEUTICS, INC.
Form 424B5
March 08, 2017

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-201339**

The information in this prospectus is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated March 8, 2017

**Prospectus Supplement (to Prospectus dated January 21, 2015)
shares**

Common Stock

We are offering shares of our common stock, \$0.001 par value per share, in this offering.

Our common stock is traded on the Nasdaq Capital Market under the symbol **TGTX**. On March 7, 2017, the last reported sale price of our common stock on the Nasdaq Capital Market was \$10.90 per share.

	Per share	Total
Public offering price	\$	\$
Underwriting discount and commissions	\$	\$
Proceeds to TG, before expenses	\$	\$

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to additional common shares.

Investing in our common stock involves a high degree of risk. See **Risk Factors beginning on page S-8.**

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the common stock on or about , 2017 only in book-entry form through the facilities of The Depository Trust Company.

Sole Book-Running Manager

Jefferies

, 2017

TABLE OF CONTENTS

Table of Contents
Prospectus Supplement

	Page
<u>About this prospectus supplement</u>	<u>i</u>
<u>Special cautionary note regarding forward-looking statements</u>	<u>ii</u>
<u>Summary</u>	<u>S-1</u>
<u>Risk factors</u>	<u>S-10</u>
<u>Use of proceeds</u>	<u>S-14</u>
<u>Capitalization</u>	<u>S-15</u>
<u>Dilution</u>	<u>S-16</u>
<u>Tax considerations</u>	<u>S-17</u>
<u>Underwriting</u>	<u>S-20</u>
<u>Legal matters</u>	<u>S-29</u>
<u>Experts</u>	<u>S-29</u>
<u>Where you can find more information</u>	<u>S-29</u>
<u>Incorporation of certain information by reference</u>	<u>S-29</u>

Prospectus

	Page
<u>TG Therapeutics, Inc.</u>	<u>1</u>
<u>The Offering</u>	<u>2</u>
<u>Forward-Looking Statements</u>	<u>3</u>
<u>Where You Can Find More Information</u>	<u>3</u>
<u>Important Information About This Prospectus</u>	<u>3</u>
<u>Incorporation of Certain Information by Reference</u>	<u>4</u>
<u>Ratio of Earnings/Deficiency to Fixed Charges</u>	<u>5</u>
<u>Description of Capital Stock</u>	<u>6</u>
<u>Description of Warrants</u>	<u>7</u>
<u>Description of Debt Securities</u>	<u>8</u>
<u>Description of Units</u>	<u>10</u>
<u>Plan of Distribution</u>	<u>11</u>
<u>Legal Matters</u>	<u>12</u>
<u>Experts</u>	<u>12</u>

TABLE OF CONTENTS

About this prospectus supplement

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein and therein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Neither we nor the underwriters have authorized anyone to provide information different from that contained in this prospectus supplement and the accompanying prospectus, including any free writing prospectus that we have authorized for use in this offering. When you make a decision about whether to invest in our common stock, you should not rely upon any information other than the information in this prospectus supplement or the accompanying prospectus, including any free writing prospectus that we have authorized for use in this offering. Neither the delivery of this prospectus supplement or the accompanying prospectus, including any free writing prospectus that we have authorized for use in this offering, nor the sale of our common stock means that information contained in this prospectus supplement and the accompanying prospectus, including any free writing prospectus that we have authorized for use in this offering, is correct after their respective dates. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled *Where You Can Find More Information* and *Incorporation of Certain Information by Reference* in this prospectus supplement.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless otherwise stated, all references in this prospectus to we, us, our, TG, the Company and similar designations refer to TG Therapeutics, Inc. and our subsidiaries. This prospectus supplement contains trademarks and trade names of TG Therapeutics, Inc., including our name and logo. Other service marks, trademarks and trade names referred to in this document are the property of their respective owners.

TABLE OF CONTENTS

Special cautionary notice regarding forward-looking statements

Certain matters discussed in this prospectus supplement and the accompanying prospectus may constitute forward-looking statements for purposes of the Securities Act of 1933, as amended, or the Securities Act, and the Securities Exchange Act of 1934, as amended, or the Exchange Act, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from the future results, performance or achievements expressed or implied by such forward-looking statements. The words anticipate, believe, estimate, may, expect and similar expressions are generally intended to identify forward-looking statements. Our actual results may differ materially from the results anticipated in these forward-looking statements due to a variety of factors, including, without limitation, those discussed under the caption Risk Factors and elsewhere in this prospectus supplement and the accompanying prospectus, as well as other factors which may be identified from time to time in our other filings with the Securities and Exchange Commission, or the SEC, or in the documents where such forward-looking statements appear. All written or oral forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements. Such forward-looking statements include, but are not limited to, statements about our:

- expectations for increases or decreases in expenses;
- expectations for the clinical and pre-clinical development, manufacturing, regulatory approval, and commercialization of our pharmaceutical product candidates or any other products we may acquire or in-license;
 - use of clinical research centers and other contractors;
- expectations as to the timing of commencing or completing pre-clinical and clinical trials, the expected outcomes of those trials and expectations as to the timing of related regulatory submissions or approvals;
- expectations for incurring capital expenditures to expand our research and development and manufacturing capabilities;
 - expectations for generating revenue or becoming profitable on a sustained basis;
 - expectations or ability to enter into marketing and other partnership agreements;
 - expectations or ability to enter into product acquisition and in-licensing transactions;
- expectations or ability to build our own commercial infrastructure to manufacture, market and sell our drug candidates;
 - acceptance of our products by doctors, patients or payors;
 - ability to compete against other companies and research institutions;
 - ability to secure adequate protection for our intellectual property;
 - ability to attract and retain key personnel;
 - availability of reimbursement for our products;
- estimates of the sufficiency of our existing cash and cash equivalents and investments to finance our operating requirements, including expectations regarding the value and liquidity of our investments;
 - stock price and its volatility; and
 - expectations for future capital requirements.

TABLE OF CONTENTS

The forward-looking statements contained in this prospectus supplement and the accompanying prospectus reflect our views and assumptions only as of the date of this prospectus supplement and the accompanying prospectus, respectively. Except as required by law, we assume no responsibility for updating any forward-looking statements.

We qualify all of our forward-looking statements by these cautionary statements. In addition, with respect to all of our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

iii

TABLE OF CONTENTS

Summary

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the Risk Factors section contained in this prospectus supplement and our consolidated financial statements and the related notes and the other documents incorporated by reference herein.

Recent Developments

On March 6, 2017, we announced positive topline results from our Phase 3 GENUINE clinical trial of TG-1101 plus ibrutinib in patients with previously treated high risk CLL. For the study, high risk was defined as having any one or more of the following: 17p deletion, 11q deletion or p53 mutation. The multicenter, randomized trial (NCT02301156), which assessed the efficacy and safety of TG-1101 plus ibrutinib, met its primary endpoint, demonstrating a statistically significant improvement in Overall Response Rate (ORR) compared to ibrutinib alone in both the Intent to Treat (ITT) population (p=0.001) and Treated population (p < 0.001). The ITT population includes all 126 randomized patients (64 in the TG-1101 + 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 + ibrutinib arm and 58 in the ibrutinib alone arm).

Overall Response Rates

	TG-1101 plus Ibrutinib	Ibrutinib	P-value
Treated Population (n)	n=59	n=58	
Overall Response Rate	80%	47%	P < 0.001

All responses were assessed by independent blinded central review using the iwCLL 2008 guidelines. Per iwCLL guidelines, responders require confirmation of response for a minimum duration of 2 months. As of the date of the analysis, each arm had responders that were awaiting confirmation visits which are scheduled to occur over the next two months. During the study it was infrequent (less than 3% in the combination arm) for initial responses to fail to be confirmed. Median follow-up for the study was approximately 12 months.

The GENUINE study was designed to demonstrate the value of adding TG-1101, a highly 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, with a minimal absolute detectable difference between the two arms of approximately 20%. The absolute difference between the arms was approximately 30% resulting in a p-value of ≤ 0.001 . Results from registration directed studies included in the ibrutinib prescribing information demonstrate single agent ibrutinib response rates ranging from 43% to 58% in patients with previously treated CLL, with the findings from the GENUINE study of 47% ORR for ibrutinib fitting well within historical experience.

In addition to ORR, observed advantages were seen for the combination in a number of secondary and other efficacy measures, including radiographic Complete Response (CR) rate, Progression Free Survival and Time to Response. Sufficient data on MRD negative status and bone marrow confirmation of radiographic CRs were not available at the time of analysis. From a safety standpoint, the combination was well tolerated with a safety profile consistent with the Phase 2 study of ublituximab plus ibrutinib recently published in the *British Journal of Haematology*.

A full analysis of the Phase 3 GENUINE data along with detailed efficacy and safety results will be submitted for presentation at a medical meeting in the first half of 2017 and we plan to request a meeting with the FDA as soon as possible thereafter to discuss the filing of the data for accelerated approval. See Risk related to our business the sufficiency of our GENUINE trial design and results are subject to FDA's discretion on page S-14 of this Prospectus Supplement.

S-1

TABLE OF CONTENTS

As of December 31, 2016, we had approximately \$45 million of cash, cash equivalents, investment securities and interest receivable. In addition, during the first quarter, we utilized our at the market sales program to sell approximately \$31 million in shares of our common stock in the open market.

Our business

We are 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. 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, 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. The Company also has pre-clinical programs seeking to develop IRAK4 (interleukin-1 receptor-associated kinase 4) inhibitors and anti-PD-L1 and anti-GITR antibodies.

We also actively evaluate complementary products, technologies and companies for in-licensing, partnership, acquisition and/or investment opportunities. To date, we have not received approval for the sale of any of our drug candidates in any market and, therefore, have not generated any product sales from our drug candidates.

TG-1101 (ublituximab)

Overview

TG-1101 (ublituximab) is a chimeric, glycoengineered monoclonal antibody that targets a unique epitope on the CD20 antigen found on the surface of B-lymphocytes developed to aid in the depletion of circulating B-cells. We hold exclusive worldwide rights to develop and commercialize TG-1101 for all indications, except for the territories of France and Belgium which have been retained by LFB Biotechnologies (LFB), and South Korea and Southeast Asia which were licensed by us to Ildong Pharmaceutical Co. Ltd (Ildong) in November 2012.

Generally, anti-CD20 antibodies are believed to exert their B-cell depleting effects through three primary mechanisms: antibody dependent cell-mediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC), and direct or programmed cell death (DCD or PCD). TG-1101 has been specifically glycoengineered to enhance ADCC activity, which should enhance its ability to deplete B-cells and may improve its anti-cancer effects when compared to Rituxan®, the leading anti-CD20 monoclonal antibody, which had worldwide sales in 2015 of more than \$7 billion.

Two single-agent, dose-escalation, Phase I studies were undertaken with TG-1101 to establish an optimal dose in patients with Non-Hodgkin's Lymphoma (NHL) and Chronic Lymphocytic Leukemia (CLL). A two part first-in-human Phase I clinical trial was first completed in France in which TG-1101 was evaluated in relapsed or refractory CLL patients at doses as high as 450mg per infusion. Subsequently, a single-agent Phase I study was undertaken in the US enrolling patients with both NHL and CLL, dosing patients up to 1200mg per infusion. In both studies, single agent therapy with TG-1101 was deemed well tolerated by treating investigators and displayed promising clinical activity in relapsed and refractory patients.

In oncology settings, anti-CD20 therapy is generally used in combination with other anti-cancer agents where it demonstrates maximum activity as opposed to single agent usage. As a result, subsequent clinical development for TG-1101 has focused on combination therapy. Currently, our priority combination trials for TG-1101 are:

The GENUINE Trial a randomized controlled Phase 3 trial evaluating TG-1101 in combination with ibrutinib, for previously treated CLL patients with high risk cytogenetics;

The UNITY-CLL Trial a randomized controlled Phase 3 trial evaluating TG-1101 in combination with TGR-1202, the Company's development stage PI3K delta inhibitor, for patients with front line and previously treated CLL;

S-2

TABLE OF CONTENTS

The UNITY-DLBCL Trial registration-directed UNITY-DLBCL Phase 2b clinical study evaluating TG-1101, in combination with TGR-1202, as well as TGR-1202 alone, in patients with previously treated Diffuse Large B-Cell Lymphoma (DLBCL); and

TG-1101 + TGR-1202 + Pembrolizumab for patients with CLL.

In addition, we have announced our intent of evaluating TG-1101 for the treatment of certain autoimmune diseases.

Currently, TG-1101 is being evaluated in a Phase 2 study for the treatment of Multiple Sclerosis (MS) and in an investigator initiated Phase 1 study for the treatment of acute neuromyelitis optica (NMO) relapses, with additional autoimmune related indications planned to be studied. Preliminary data from this Phase 1 study in NMO was presented at the 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), in London, UK in September 2016. Data from the poster presentation demonstrated that TG-1101 was well tolerated with minimal adverse events (AEs) observed and rapid and robust B-cell depletion observed following a single 450 mg infusion of TG-1101. In August 2016, it was also announced that TG-1101 received orphan drug designation for the Treatment of Neuromyelitis Optica and Neuromyelitis Optica Spectrum Disorder.

Manufacturing of TG-1101 is currently performed by our partner, LFB Biotechnologies and a secondary contract manufacturer based in the US.

Pre-Clinical Data Overview

The mechanism of action of anti-CD20 antibodies, including rituximab and TG-1101 has been elucidated and detailed in numerous academic and clinical studies. Upon conjugation of the antibody to the CD20 surface antigen, rituximab has been found to deplete B-lymphocytes through three primary mechanisms: ADCC, CDC, and DCD or PCD.

Antibody dependent cellular cytotoxicity, or ADCC, is a mechanism that is dependent on interactions between the Fc region of the antibody and the Fc R receptors on immune system effector cells, most notably the Fc RIIIA (CD16) receptor found on NK cells. These interactions trigger cells to release cytotoxic molecules and proteases resulting in B-cell death. TG-1101 is a third generation, type I chimeric IgG1 monoclonal antibody with a glycoengineered Fc region designed specifically to induce higher ADCC activity in comparison to rituximab, which has been demonstrated in pre-clinical models.

Clinical Data Overview and Recent Developments

Single Agent TG-1101 in Relapsed/Refractory NHL & CLL

Our first US based trial entitled An Open Label Phase I/II Trial of the Efficacy and Safety of TG-1101 in Patients with B-cell Non-Hodgkin's Lymphoma who have Relapsed or are Refractory After CD20 Directed Antibody Therapy, was launched in the third quarter of 2012. In July 2014, this trial completed enrollment at 35 patients, of which 12 patients were included in the dose escalation component and 23 patients in various expansion cohorts. All enrolled patients were relapsed or refractory to Rituxan® or a Rituxan® containing regimen, and in most cases multiple other lines of therapy. Dr. Owen O'Connor, Professor of Medicine and Director, Center for Lymphoid Malignancies at New York Presbyterian Columbia Medical Center was the Principal Investigator for the multi-center study.

Preliminary data from this study was presented at the 50th American Society of Clinical Oncology (ASCO) 2014 Annual Meeting in Chicago, IL, and was recently published in full in the British Journal of Haematology and is summarized below:

TG-1101 was well tolerated at all dose levels tested in the 35 patients evaluable for safety, with Day 1 infusion related reactions (IRR) being the most frequently reported adverse event. The combined overall response rate (ORR) for the

Phase 1 dose escalation component and expansion cohorts was 45% (32% PR, 13% CR) among the 31 rituximab relapsed/refractory patients evaluable for efficacy at the time of the presentation. TG-1101 displayed marked clinical activity as a single agent in a variety of lymphoma subtypes, reporting a 50% (3/6)

S-3

TABLE OF CONTENTS

response rate in patients with CLL and 53% (10/19) response rate in patients with indolent NHL (21% CR, 32% PR). Responses were durable, with a median duration of response of 9.2 months and duration of progression free survival (PFS) of 7.7 months (n=31) amongst evaluable patients.

TG-1101 in Combination with TGR-1202 for Relapsed/Refractory NHL & CLL

In November 2013, we initiated a multi-center, Phase I study to evaluate the safety and efficacy of the combination of TG-1101 and TGR-1202, the Company's novel, once per day, PI3K delta inhibitor, for patients with relapsed and/or refractory CLL and NHL. In this study, dosing of TGR-1202 commenced at 800mg (initial formulation) once per day (QD) with dose escalation proceeding in a 3+3 design. Dose-escalation up to 1200mg micronized formulation has been completed and expansion cohorts were also evaluated at various doses. Additional cohorts were added to this study to explore the triple therapy combination of TG-1101, TGR-1202, and ibrutinib and the triple therapy of TG-1101, TGR-1202, and bendamustine.

The MD Anderson Cancer Center is the lead center for the trial with Nathan Fowler, MD, Assistant Professor and Co-Director of Clinical Research in the Department of Lymphoma, as the Study Chair for the NHL patient group and Susan O'Brien, MD, formerly of MD Anderson and now Professor and Medical Director for Cancer Clinical Trials and Research at UC Irvine as the Study Chair for the CLL patient group.

Preliminary data from this study was presented at the 57th Annual American Society of Hematology (ASH) meeting held in December 2015 and is summarized below:

The combination of TG-1101 and TGR-1202 was well tolerated in the 71 patients evaluable for safety, with only 8% of patients discontinuing due to an adverse event. Notably, the only Grade 3/4 adverse event occurring in > 5% of patients was neutropenia. As of the data presentation, twenty-six patients had been on the combination of TG-1101 plus TGR-1202 for 6+ months, with no events of colitis reported. The combination displayed marked clinical activity in a variety of lymphoma subtypes, reporting an 80% (8/10) response rate in patients with CLL, a 71% (12/17) response rate in patients with indolent NHL, and a 35% (6/17) response rate in patients with DLBCL and Richter's Transformation. The data from this study supports the current Phase 3 UNITY-CLL study of TG-1101 + TGR-1202 in CLL.

Preliminary data from the combination of TG-1101 + TGR-1202 + ibrutinib and TG-1101 + TGR-1202 + bendamustine were presented at the American Society of Clinical Oncology (ASCO) 2015 meeting and the American Society of Hematology (ASH) 2016 meeting respectively. Both combinations demonstrated acceptable levels of tolerability with promising activity and continue to enroll as of today.

TG-1101 in Combination with Ibrutinib for Relapsed/Refractory MCL & CLL

In December 2013, we initiated a multi-center Phase 2 clinical trial to evaluate the safety and efficacy of the combination of TG-1101 and ibrutinib for patients with CLL and MCL. This is the first clinical trial evaluating the combination of TG-1101 and ibrutinib, an oral Bruton's Tyrosine Kinase (BTK) inhibitor.

TG Therapeutics partnered with the US Oncology Network and other select centers throughout the United States on the study, with Jeff Sharman, MD, Medical Director for Hematology Research, US Oncology Network, as the Study Chair. This trial has completed enrollment.

Final data from this study was presented on the MCL cohort at the 57th Annual American Society of Hematology (ASH) meeting held in December 2015, and on the CLL cohort at the 13th International Congress on Malignant

Lymphoma (ICML), held in June 2015 and recently published in full in the *British Journal of Haematology* and is summarized below:

In the CLL cohort, TG-1101 in combination with ibrutinib was well tolerated in the 45 patients evaluable for safety, with day 1 infusion related reactions (IRR) being the most frequently reported adverse event (regardless of causality). In the MCL cohort, the combination was well tolerated in the 15 patients evaluable for safety, with fatigue being the most frequently reported adverse event (regardless of causality). Overall, in both CLL and MCL, aside from day 1 IRR, the addition of TG-1101 did not appear to alter the safety profile seen historically with single agent ibrutinib. Of the 60 patients treated, 41 CLL and 15 MCL patients were evaluable for

S-4

TABLE OF CONTENTS

response. The combination displayed marked clinical activity, reporting an 88% (35/41) response rate in patients with CLL, a 95% (19/21) response rate in those CLL patients with high-risk cytogenetics, and an 87% (13/15) response rate in patients with MCL.

TG-1101 + Ibrutinib Phase 3 Study Program The GENUINE Trial

The GENUINE trial is a randomized controlled clinical trial in patients with previously treated CLL with specific high-risk cytogenetic abnormalities, with patients randomized to receive either TG-1101 plus ibrutinib or ibrutinib alone. In October 2016, we announced revisions to the design of the GENUINE study to accelerate its completion. Initially the study was being conducted pursuant to a Special Protocol Assessment (SPA) with the U.S. Food and Drug Administration (FDA), and was designed to enroll approximately 330 patients, with a two-part analysis of both overall response rate (ORR) and progression-free survival (PFS). The trial was amended in October 2016 to enroll approximately 120 patients, with the PFS analysis component removed. Following the revisions, the sole primary endpoint of the study is now ORR, and the SPA is no longer in effect. We have communicated with the FDA regarding our intention to file a Biologics Licensing Application (BLA) for accelerated approval and the FDA has agreed that a pre-BLA meeting can be requested based on ORR data from the GENUINE study.

In December, 2016 we announced that the study had completed enrollment, and in March 2017 we announced topline data from the GENUINE study. The study, which assessed the efficacy and safety of TG-1101 plus ibrutinib, met its primary endpoint, demonstrating a statistically significant improvement in Overall Response Rate (ORR) compared to ibrutinib alone in both the Intent to Treat (ITT) population ($p=0.001$) and Treated population ($p < 0.001$). The ITT population includes all 126 randomized patients (64 in the TG-1101 + 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 + ibrutinib arm and 58 in the ibrutinib alone arm). Amongst the treated population, the overall response rate for ublituximab + ibrutinib was 80% compared to 47% for ibrutinib alone. The combination was well tolerated with a safety profile consistent with the Phase 2 study of ublituximab plus ibrutinib recently published in the *British Journal of Haematology*. Per iwCLL guidelines, responders require confirmation of response for a minimum duration of 2 months. As of the date of the analysis, each arm had responders that were awaiting confirmation visits which are scheduled to occur over the next two months. During the study it was infrequent (less than 3% in the combination arm) for initial responses to fail to be confirmed.

Results from registration directed studies included in the ibrutinib prescribing information demonstrate single agent ibrutinib response rates ranging from 43% to 58% in patients with previously treated CLL, with the findings from the GENUINE study of 47% ORR for ibrutinib fitting well within historical experience. A full analysis of the Phase 3 GENUINE data along with detailed efficacy and safety results will be submitted for presentation at a medical meeting in the first half of 2017 and we plan to request a meeting with the FDA as soon as possible thereafter to discuss the filing of the data for accelerated approval. See Risk related to our business the sufficiency of our GENUINE trial design and results are subject to FDA's discretion on page S-14 of this Prospectus Supplement.

TG-1101 in Combination with TGR-1202 Phase 3 Study Program The UNITY-CLL Trial

In September 2015, we reached an agreement with the FDA regarding an SPA on the design, endpoints and statistical analysis approach of a Phase 3 clinical trial for the proprietary combination of TG-1101 plus TGR-1202, for the treatment of CLL. The SPA provides agreement that the Phase 3 trial design adequately addresses objectives that, if met, would support the regulatory submission for drug approval of both TG-1101 and TGR-1202 in combination.

The Phase 3 trial, called the UNITY-CLL trial, is a randomized controlled clinical trial that includes two key objectives: first, to demonstrate contribution of each agent in the TG-1101 + TGR-1202 regimen (the combination

sometimes referred to as 1303), and second, to demonstrate superiority in Progression Free Survival (PFS) over the standard of care to support the submission for full approval of the combination. The study will randomize patients into four treatment arms: TG-1101 + TGR-1202, TG-1101 alone, TGR-1202 alone, and an active control arm of obinutuzumab (GAZYVA®) + chlorambucil. An early interim analysis will

S-5

TABLE OF CONTENTS

assess contribution of each single agent in the TG-1101 + TGR-1202 combination regimen, which, if successful, will allow early termination of both single agent arms. A second interim analysis will be conducted following full enrollment into the study, which, if positive, we plan to utilize for accelerated approval. Assuming early termination of the TG-1101 and TGR-1202 single agent arms, the study will enroll approximately 450 patients.

TG-1101 in Combination with TGR-1202 Phase 2b Registration-Directed Program The UNITY-DLBCL Trial

In June 2016, we commenced a registration-directed UNITY-DLBCL Phase 2b clinical study evaluating TG-1101 in combination with TGR-1202, as well as TGR-1202 alone, in patients with previously treated DLBCL.

The study, entitled A Phase 2b Randomized Study to Assess the Efficacy and Safety of the Combination of Ublituximab + TGR-1202 and TGR-1202 alone in Patients with Previously Treated Diffuse Large B-Cell Lymphoma, is being led by Owen A. O'Connor, MD, PhD, Professor of Medicine and Experimental Therapeutics, and Director of the Center for Lymphoid Malignancies at Columbia University Medical Center. The primary objective of the study is to assess the efficacy of TGR-1202 alone and in combination with TG-1101 in patients with previously treated DLBCL as measured by Overall Response Rate (ORR). The study will also provide important information as to the contribution of each agent, TGR-1202 and TG-1101, to the combination regimen of both agents. In addition to monitoring for safety and efficacy this study will analyze the impact of cell of origin (GCB vs. non-GCB), mutational status and select biomarkers of efficacy.

Single Agent TG-1101 in Relapsing Forms of Multiple Sclerosis

In May 2016, we commenced our first study of TG-1101 in patients with relapsing remitting multiple sclerosis (RRMS), a chronic demyelinating disease of the central nervous system (CNS).

The study, entitled A Placebo-Controlled Multi-Center Phase 2 Dose Finding Study of Ublituximab, a Third-Generation Anti-CD20 Monoclonal Antibody, in Patients with Relapsing Forms of Multiple Sclerosis, is being led by Edward Fox, MD, PhD, Director of the Multiple Sclerosis Clinic of Central Texas and Clinical Assistant Professor at the University of Texas Medical Branch in Round Rock, TX. The primary objective of the study is to determine the optimal dosing regimen for TG-1101 with a focus on accelerating infusion times. In addition to monitoring for safety and tolerability at each dosing cohort, B-cell depletion and established MS efficacy endpoints will also be evaluated.

In January 2017, we announced the completion of enrollment into Part 1 of this study and B-cell depletion data from patients treated to date. Part 1 of the study explored TG-1101 at an initial dose of 600 mg administered as a 150 mg infusion on day 1 and 450 mg infusion on day 15, followed by either 450 mg or 600 mg at week 24. The day 15 and week 24 doses were subject to accelerated infusion times by cohort, down to a 1-hour infusion by cohort 3. The median B-cell depletion for all patients in Part 1 was 99% and TG-1101 was well-tolerated with no grade 3/4 adverse events reported, including in patients receiving the one-hour infusion at the target Phase 3 dose and infusion rate. For Part 2 of the trial, the Company has added expansion cohorts and will explore accelerated dosing of the initial 150mg dose.

TGR-1202

Overview

The phosphoinositide-3-kinases (PI3Ks) are a family of enzymes involved in various cellular functions, including cell proliferation and survival, cell differentiation, intracellular trafficking, and immunity. There are four isoforms of PI3K (alpha, beta, delta, and gamma), of which the delta (lgd) isoform is strongly expressed in cells of hematopoietic origin, and often implicated in B-cell related lymphomas.

TGR-1202 is an orally available PI3K delta inhibitor with nanomolar potency to the delta isoform and high selectivity over the alpha, beta, and gamma isoforms. TGR-1202 has demonstrated activity in several pre-clinical models and primary cells from patients with various hematologic malignancies.

S-6

TABLE OF CONTENTS

We hold exclusive rights to develop and commercialize TGR-1202 for all indications worldwide, except India which has been retained by Rhizen Pharmaceuticals, SA.

The Company's Investigational New Drug (IND) application for TGR-1202 was accepted by the FDA in December 2012 and a first in-human Phase I clinical trial was initiated in January 2013.

Updates for TGR-1202

In August 2016, we announced that TGR-1202 had received orphan drug designation for the treatment of CLL.

In October 2016, a manuscript titled, "Silencing c-Myc Translation as a Therapeutic Strategy through Targeting PI3K Delta and CK1 Epsilon in Hematological Malignancies," was published online in the First Edition section of Blood, the Journal of the American Society of Hematology. The publication presents preclinical data describing the synergy of 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 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).

Clinical Data Overview and Recent Developments

Initial clinical development of TGR-1202 was focused on establishing preliminary safety and efficacy in a wide variety of hematologic malignancies. Upon identification of safe and active doses of TGR-1202, a combination clinical trial program was opened, exploring TGR-1202 in combination with a variety of agents. In addition to the previously described studies in combination with TG-1101, our current combination clinical trials that are ongoing or have been completed for TGR-1202 include:

TGR-1202 in combination with the anti-CD20 antibody, obinutuzumab (GAZYVA®) and chlorambucil in patients with CLL;

TGR-1202 in combination with the anti-CD30 antibody drug conjugate, brentuximab vedotin (ADCETRIS®, in patients with relapsed or refractory Hodgkin's lymphoma;

TGR-1202 in combination with the BTK inhibitor, ibrutinib, in patients with previously treated CLL and MCL; and TGR-1202 in combination with the JAK inhibitor, ruxolitinib (JAKAFI®), in patients with previously treated Myelofibrosis or Polycythemia Vera.

In addition, given the favorable safety profile demonstrated to date, a trial of TGR-1202 monotherapy in patients with CLL who were previously intolerant to prior BTK or PI3K inhibitor therapy is also underway.

Single Agent TGR-1202 in Patients with Relapsed/Refractory Hematologic Malignancies

In January 2013, the Company initiated a Phase I, open label, multi-center, first-in-human clinical trial of TGR-1202 in patients with hematologic malignancies. The study entitled TGR-1202-101, "A Phase I Dose Escalation Study Evaluating the Safety and Efficacy of TGR-1202 in Patients with Relapsed or Refractory Hematologic Malignancies," is being run in collaboration with the Sarah Cannon Research Institute in Nashville, TN with Howard Skip Burris, MD, Executive Director, Drug Development as the acting Study Chair. Enrollment is open to patients with relapsed or refractory NHL, CLL, and other select hematologic malignancies. As of February 2016, this study has closed to enrollment.

Data from this ongoing Phase I study was most recently presented at the 57th Annual American Society of Hematology (ASH) meeting held in December 2015, with updated data presented as part of an integrated analysis as described below.

TGR-1202 Long-term Follow-up Integrated Analysis in Patients with Relapsed/Refractory Hematologic Malignancies

S-7

TABLE OF CONTENTS

In June 2016, at the 52nd Annual Meeting of the American Society of Clinical Oncology (ASCO) and at the 21st Congress of the European Hematology Association (EHA), the Company presented integrated data with long term follow-up from 165 patients exposed to TGR-1202 monotherapy or the combination of TGR-1202 plus TG-1101, which continued to demonstrate high response rates in CLL, NHL, and DLBCL coupled with a favorable safety profile.

TGR-1202 in Combination with obinutuzumab and chlorambucil in patients with CLL

In March 2014, the Company initiated a Phase I/Ib, open label, multi-center, clinical trial of TGR-1202 in combination with obinutuzumab and chlorambucil in patients with CLL, both treatment naïve and relapsed. The study entitled TGR-GA-106, A Multi-center Phase I/Ib Study Evaluating the Efficacy and Safety of TGR-1202, a Novel PI3K Delta Inhibitor, in Combination with Obinutuzumab and Chlorambucil in Patients with Chronic Lymphocytic Leukemia (CLL), is being led by Dr. Daruka Mahadevan of the West Clinic in Memphis, TN. As of February 2016, this study has completed enrollment.

Data from this study was presented at the 57th Annual American Society of Hematology (ASH) meeting held in December 2015.

TGR-1202 Combination Trials

TGR-1202 is being evaluated in combination with the anti-CD30 antibody drug conjugate, brentuximab vedotin, in patients with relapsed or refractory Hodgkin's lymphoma; in combination with the BTK inhibitor, ibrutinib, in patients with CLL and MCL; and in combination with the JAK inhibitor, ruxolitinib, in patients with Myelofibrosis or Polycythemia Vera. Additional investigator sponsored trials are also underway which are combining TGR-1202 with other approved agents for the treatment of B-cell malignancies.

Preliminary data from studies evaluating TGR-1202 + brentuximab vedotin and TGR-1202 + ibrutinib were presented at the 58th Annual American Society of Hematology (ASH) meeting held in December 2016. Both combinations appeared well tolerated. In particular, the combination of TGR-1202 + ibrutinib resulted in an 88% (15 of 17) Overall Response Rate (ORR) (including Complete Response (CR), Partial Response (PR), and Partial Response with lymphocytosis (PR-L)) in patients with CLL, with 1 patient achieving a bone marrow confirmed CR and 5 patients with a > 80% nodal reduction, nearing radiographic CR.

It is anticipated that results from these studies will be presented or updated at future medical conferences.

TGR-1202 in Solid Tumors

In addition to the exploration of TGR-1202 in various hematologic malignancies, a study was opened in October 2015 to evaluate TGR-1202 as a single agent as well as in combination with various chemotherapies for the treatment of select solid tumors. The study, entitled TGR-1202-102, A Phase I Study Evaluating the Safety and Efficacy of TGR-1202 Alone and in Combination with either nab-paclitaxel + Gemcitabine or with FOLFOX in Patients with Select Relapsed or Refractory Solid Tumors is being run in collaboration with the Sarah Cannon Research Institute in Nashville, TN with Johanna Bendell, MD, Director of GI Oncology Research as the acting study chair.

Company information

Our principal executive offices are located at 2 Gansevoort St., 9th Floor, New York, New York 10014, and our telephone number is 212-554-4484. We maintain a website on the Internet at www.tgtherapeutics.com and our e-mail address is info@tgtxinc.com. Our Internet website, and the information contained on it, are not to be considered part of this prospectus supplement or the accompanying prospectus. For further information regarding us and our financial information, you should refer to our recent filings with the SEC. See [Where You Can Find More Information](#) and [Incorporation of Certain Information by Reference](#).

S-8

TABLE OF CONTENTS

The offering

Issuer

TG Therapeutics, Inc.

Common stock offered by us

shares

Common stock to be outstanding after the offering

shares

Use of Proceeds

We intend to use the net proceeds of this offering for the continued development of TG-1101 and TGR-1202, the potential in-license, acquisition, development and commercialization of other pharmaceutical products, research and development activities and for general corporate purposes. See Use of Proceeds on page S-14.

Risk Factors

See Risk Factors beginning on page S-10 for a discussion of factors that you should consider before buying shares of our common stock.

Nasdaq Capital Market Symbol

TGTX

The number of shares of common stock to be outstanding after the offering assumes no exercise of the underwriters option to purchase additional shares of common stock and is based on 54,724,581 shares of common stock outstanding as of September 30, 2016.

The number of shares of common stock to be outstanding after this offering does not take into account:

1,142,208 shares of common stock issuable upon the exercise of outstanding warrants with a weighted average exercise price of \$2.38 per share;

15,133 shares of common stock issuable upon the conversion of outstanding notes payable with a weighted average conversion price of \$1,125 per share; and

an aggregate of 3,938,403 shares of common stock reserved for future issuance under our stock option and incentive plans; and

3,223,555 shares sold under our at the market sales program during the fourth quarter of 2016 and the first quarter of 2017.

S-9

TABLE OF CONTENTS

Risk factors

Investment in our common stock involves risks. Before deciding whether to invest in our common stock, you should consider carefully the risk factors discussed below and those contained in the section entitled Risk Factors contained in our Annual Report on Form 10-K for the year ended December 31, 2015 and our Quarterly Reports for the periods ended March 31, 2016, June 30, 2016 and September 30, 2016, as filed with the SEC on December 31, 2015, May 10, 2016, August 9, 2016 and November 9, 2016, respectively, which are incorporated herein by reference in their entirety, as well as any amendment or update to our risk factors reflected in subsequent filings with the SEC.

If any of the risks or uncertainties described in our SEC filings actually occurs, our business, financial condition, results of operations or cash flow could be materially and adversely affected. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks related to this offering

Future sales or other issuances of our common stock could depress the market for our common stock.

Sales of a substantial number of shares of our common stock, or the perception by the market that those sales could occur, could cause the market price of our common stock to decline or could make it more difficult for us to raise funds through the sale of equity in the future.

In connection with this offering, we, our directors and officers, and certain of our significant shareholders have entered into lock-up agreements for a period of 90 days following this offering (which period may be extended under certain circumstances). We and our directors and officers may be released from lock-up prior to the expiration of the lock-up period at the sole discretion of Jefferies. See Underwriting. Upon expiration or earlier release of the lock-up, we and our directors and officers may sell shares into the market, which could adversely affect the market price of shares of our common stock.

Future issuances of common stock could further depress the market for our common stock.

If we make one or more significant acquisitions in which the consideration includes stock or other securities, our stockholders' holdings may be significantly diluted. In addition, stockholders' holdings may also be diluted if we enter into arrangements with third parties permitting us to issue shares of common stock in lieu of certain cash payments upon the achievement of milestones.

Our stock price can be volatile, which increases the risk of litigation, and may result in a significant decline in the value of your investment.

The trading price of our common stock is likely to be highly volatile and subject to wide fluctuations in price in response to various factors, many of which are beyond our control. These factors include:

developments concerning our drug candidates, including the safety and efficacy results from clinical trials and regulatory filings and approvals;

announcements of technological innovations by us or our competitors;
introductions or announcements of new products by us or our competitors;
announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments involving us
or our competitors;

changes in financial estimates by securities analysts;
actual or anticipated variations in quarterly or annual operating results;
expectations regarding our financial condition;

S-10

TABLE OF CONTENTS

expiration or termination of licenses, research contracts or other collaboration agreements;
conditions or trends in the regulatory climate and the biotechnology and pharmaceutical industries;
changes in the market valuations of similar companies;
negative comments and sentiment in the media; and
additions or departures of key personnel.

In addition, equity markets in general, and the market for biotechnology and life sciences companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of companies traded in those markets. These broad market and industry factors may materially affect the market price of our common stock, regardless of our development and operating performance. In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation has often been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management's attention and resources, which could seriously harm our business.

On January 6, 2017, a purported securities class action complaint was filed in New York federal court against the Company and certain of its directors, officers or consultants on behalf of all shareholders who purchased or otherwise acquired TG Therapeutics common stock between September 15, 2014 and October 12, 2016 (the Class Period). The case is captioned *John Lyon v. TG Therapeutics, Michael S. Weiss, Sean A. Power and Robert Niecestro*, Case No. 1:17-cv-00112-VM (S.D.N.Y.). The complaint alleges that, throughout the Class Period and including on October 13, 2016, that the Company had filed an amended protocol for its GENUINE Phase 3 trial, various statements made by the Company regarding its GENUINE Phase 3 trial were materially false or misleading when made in violation of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder. On January 24, 2017, a second purported securities class action complaint was filed in New York federal court against the Company and certain of its directors, officers or consultants on behalf of all shareholders also on behalf of all shareholders who purchased or otherwise acquired TG Therapeutics common stock between September 15, 2014 and October 12, 2016. The case is captioned *Kenneth C. Wyzgoski v. TG Therapeutics, Michael S. Weiss, Sean A. Power and Robert Niecestro*, Case No. 1:17-cv-00508-VM (S.D.N.Y.). The claims and allegations in the Wyzgoski complaint are substantively identical to those in the *Lyon* case. Both actions remain pending and are in the early stages of litigation.

Certain anti-takeover provisions in our charter documents and Delaware law could make a third-party acquisition of us difficult. This could limit the price investors might be willing to pay in the future for our common stock.

Provisions in our amended and restated certificate of incorporation and restated bylaws could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, or control us. These factors could limit the price that certain investors might be willing to pay in the future for shares of our common stock. Our amended and restated certificate of incorporation allows us to issue preferred stock without the approval of our stockholders, including pursuant to our shareholder rights plan. The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to the holders of our common stock or could adversely affect the rights and powers, including voting rights, of such holders. In certain circumstances, such issuance could have the effect of decreasing the market price of our common stock. Our shareholder rights plan could be used by our board to deter any third party offer to acquire a significant portion of our common stock, even an offer at a premium to the market price. Our restated bylaws eliminate the right of stockholders to call a special meeting of stockholders, which could make it more difficult for stockholders to effect certain corporate actions. Any of these provisions could also have the effect of delaying or preventing a change in control.

TABLE OF CONTENTS

We have broad discretion to use the net proceeds from this offering and our investment of these proceeds pending any such use may not yield a favorable return.

Our management has broad discretion as to how to spend the proceeds from this offering and may spend these proceeds in ways with which our stockholders may not agree. Pending any such uses, we plan to invest the net proceeds of this offering in short-term and long-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

You will experience immediate and substantial dilution.

Since the public offering price of the shares of common stock offered pursuant to this prospectus supplement and the accompanying prospectus is higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. See "Dilution" in this prospectus supplement for a more detailed discussion of the dilution you will incur if you purchase shares of our common stock in this offering.

Risk related to our business

The sufficiency of our GENUINE trial design and results are subject to FDA's discretion.

On March 6, 2017, we announced topline data from our Phase 3 GENUINE clinical trial of TG-1101 in combination with ibrutinib as a treatment for patients with previously treated high risk Chronic Lymphocytic Leukemia, or CLL. This trial, as originally designed, was prepared under FDA's Special Protocol Assessment (SPA) procedures, in which FDA agrees in advance of commencement of a Phase III clinical trial that the trial's design, clinical endpoints and statistical analyses will constitute a pivotal study for purposes of regulatory approval, assuming that the resulting data is sufficiently favorable. In October 2016, we amended the protocol, which had the effect of reducing the number of enrolled patients to approximately 120 and eliminating progression-free survival as a primary endpoint, leaving overall response rate as the sole primary endpoint. In doing so, we invalidated the trial's SPA.

We believe that the trial design and the resulting data could support FDA approval, but that is a question wholly within FDA's discretion to determine. Whether or not FDA accepts the data for filing will depend on FDA's views on the adequacy of the filing. Consequently, there can be no assurance that FDA will approve TG-1101, or even whether FDA will agree to meet with us to discuss the matter.

A critical area of inquiry in the GENUINE clinical trial will be the overall response rate observed. As per applicable guidelines, responders require confirmation of response for a minimum duration of two months. As of the date of analysis, nine patients that demonstrated a response in the combination therapy arm of the trial were awaiting confirmation visits, which are expected to occur over the next two months. During the study, less than 3% of patients who demonstrated a response in the combination therapy arm of the trial failed to be a confirmed response at subsequent follow-up. Nevertheless, if one or more of the nine patients awaiting confirmation do not maintain their response at the next checkpoint, our previously reported results could be adversely affected, perhaps materially so, which could adversely affect the likelihood of regulatory approval.

Any product candidates we may advance through clinical development are subject to extensive regulation, which can be costly and time consuming, cause unanticipated delays or prevent the receipt of the required approvals or any accelerated or fast track status to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates or any future product candidates are subject to extensive regulation by the FDA in the United States and by comparable health authorities worldwide or in foreign markets. In the United States, we are not permitted to market our product candidates until we receive approval of a BLA or NDA from the FDA. The process of obtaining BLA and NDA approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. Approval policies or regulations may change and the FDA has substantial discretion in the pharmaceutical approval process, including the ability to delay, limit or deny approval of a product candidate

S-12

TABLE OF CONTENTS

for many reasons. Even with fast track or priority review status which we intend to seek for our product candidates where possible, including with regard to TG-1101, such designations do not necessarily mean a faster development process or regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. In addition, the FDA may require post-approval clinical trials or studies which also may be costly.

S-13

TABLE OF CONTENTS

Use of proceeds

The net proceeds to us from the sale of shares of our common stock will be approximately \$ million after deducting underwriting discounts and estimated offering expenses payable by us.

We expect to use the net proceeds from this offering:

to fund the ongoing development of TG-1101 and TGR-1202;
to potentially in-license, acquire, develop and commercialize additional drug candidates;
for research and development activities; and
for general corporate purposes.

The timing and amounts of our actual expenditures will depend on several factors, including the progress of our research and development programs, the results of other pre-clinical and clinical studies and the timing and costs of regulatory approvals. Pending the uses described above, we will invest the net proceeds in short-term and long-term, investment grade, interest-bearing securities.

Dividend policy

We have never declared or paid any cash dividends on our common stock and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors.

S-14

TABLE OF CONTENTS**Capitalization**

The following table sets forth our capitalization as of September 30, 2016:

on an actual basis; and

on an as adjusted basis to reflect the sale of the shares of common stock offered by us in this offering after deducting underwriting discounts and estimated offering expenses payable by us.

You should read this information together with our financial statements and the notes to those statements incorporated by reference into this prospectus supplement and the related prospectus.

September 30, 2016 (unaudited) (in thousands, except share data)	Actual	As Adjusted
Cash and cash equivalents, investment securities and interest receivable	60,710,595	
Stockholders' equity:		
Preferred stock, \$0.001 par value per share, 10,000,000 shares authorized; none issued and outstanding, actual and as adjusted		
Common stock, \$0.001 par value per share, 150,000,000 shares authorized; 54,765,890 shares actual and shares as adjusted, issued; 54,724,581 shares actual and shares as adjusted, issued and outstanding	54,766	
Contingently issuable shares	6	
Additional paid-in capital	269,646,963	
Treasury stock, at cost, 41,309 shares, actual and as adjusted	(234,337)	
Accumulated deficit	(212,712,677)	
Total stockholders' equity	56,754,721	
Total capitalization	56,871,847	

The table assumes no exercise of the underwriters' option to purchase additional shares of common stock and excludes the following shares:

1,142,208 shares of common stock issuable upon the exercise of outstanding warrants with a weighted average exercise price of \$2.38 per share;

15,133 shares of common stock issuable upon the conversion of outstanding notes payable with a weighted average conversion price of \$1,125 per share; and

an aggregate of 3,938,403 shares of common stock reserved for future issuance under our stock option and incentive plans; and

3,223,555 shares sold under our at the market sales program during the fourth quarter of 2016 and the first quarter of 2017.

S-15

TABLE OF CONTENTS**Dilution**

Purchasers of the shares offered by this prospectus supplement and the accompanying prospectus will suffer immediate and substantial dilution in the net tangible book value per share of the common stock they purchase. Net tangible book value per share represents the amount of total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of September 30, 2016. Our net tangible book value as of September 30, 2016 was approximately \$55,955,330, or \$1.02 per share of our common stock.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the sale of shares of common stock in this offering at the public offering price of \$ per share, and after deducting the underwriting discount and the estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2016 would have been approximately \$ per share of common stock. This represents an immediate increase in net tangible book value of \$ per share of common stock to our existing stockholders and an immediate dilution in net tangible book value of \$ per share of common stock to purchasers in this offering. The following table illustrates this per share dilution:

Public offering price per share		\$
Net tangible book value per share as of September 30, 2016	\$ 1.02	
Increase per share attributable to this offering	\$	
As adjusted net tangible book value per share as of September 30, 2016 after this offering		\$
Dilution per share to new investors participating in this offering		\$

The above table is based on 54,724,581 shares of common stock outstanding as of September 30, 2016, assumes no exercise of the underwriters' option to purchase additional shares of common stock and excludes, as of that date:

1,142,208 shares of common stock issuable upon the exercise of outstanding warrants with a weighted average exercise price of \$2.38 per share;

15,133 shares of common stock issuable upon the conversion of outstanding notes payable with a weighted average conversion price of \$1,125 per share; and

an aggregate of 3,938,403 shares of common stock reserved for future issuance under our stock option and incentive plans; and

3,223,555 shares sold under our at the market sales program during the fourth quarter of 2016 and the first quarter of 2017.

If the underwriters exercise in full their option to purchase additional shares of our common stock, the as adjusted net tangible book value after this offering would be \$ per share, representing an increase in net tangible book value of \$ per share to existing stockholders and immediate dilution in net tangible book value of \$ per share to purchasers in this offering.

To the extent that any options or warrants are exercised, new options are issued under our equity incentive plans or we otherwise issue additional shares of common stock in the future at a price less than the public offering price, there will be further dilution to new investors.

TABLE OF CONTENTS

Tax considerations

The following is a summary of material United States federal income tax consequences relating to the acquisition, ownership and disposition of our common stock as of the date hereof. Except where noted, this summary deals only with our common stock that is held as a capital asset by a non-U.S. holder (as defined below).

For purposes of this summary, a non-U.S. holder means a person (other than a partnership or any other entity treated as a partnership for United States federal income tax purposes) that is not for United States federal income tax purposes any of the following:

an individual citizen or resident of the United States;

a corporation (or any other entity treated as a corporation for United States federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia;

an estate the income of which is subject to United States federal income taxation regardless of its source; or a trust if it (1) is subject to the primary supervision of a court within the United States and one or more United States persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable United States Treasury regulations (Treasury Regulations) to be treated as a United States person.

This summary is based upon provisions of the Internal Revenue Code of 1986, as amended (the Code) and Treasury Regulations, administrative rulings and judicial decisions currently in effect, all as of the date hereof and all subject to change at any time, possibly with retroactive effect, or to different interpretation by the Internal Revenue Service

(IRS). This summary does not address all aspects of United States federal taxes and does not address any foreign, state, local or other tax considerations that may be relevant to non-U.S. holders in light of their personal circumstances. In addition, this summary does not represent a detailed description of the United States federal income tax consequences applicable to holders that are subject to special treatment under the United States federal income tax laws (including a holder that is a United States expatriate, controlled foreign corporation, passive foreign investment company, real estate investment trust, regulated investment company, dealer in securities or currencies, financial institution, tax-exempt entity, insurance company, person holding our common stock as part of a hedging, integrated, conversion or constructive sale transaction or a straddle, trader in securities that elects to use a mark-to-market method of accounting, person liable for the alternative minimum tax, person who acquired our common stock as compensation for services, or a partnership or other pass-through entity, or partner in a partnership or beneficial owner of a pass-through entity that holds our common stock for United States federal income tax purposes). We cannot provide assurance that a change in law will not alter significantly the tax considerations that we describe in this summary.

If a partnership holds our common stock, the tax treatment of a partner will generally depend upon the status of the partner and the activities of the partnership. Non-U.S. holders that are partners of a partnership holding our common stock should consult their tax advisors.

Non-U.S. holders considering the purchase of our common stock should consult their own tax advisors concerning the particular United States federal income and estate tax consequences of the ownership of our common stock, as well as the consequences arising under the laws of any other taxing jurisdiction.

S-17

TABLE OF CONTENTS

Dividends

Distributions paid on our common stock will be taxable as dividends to the extent paid out of current or accumulated earnings and profits, as determined under United States federal income tax principles. Dividends paid to a non-U.S. holder of our common stock generally will be subject to withholding of United States federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. However, dividends that are effectively connected with the conduct of a trade or business by the non-U.S. holder within the United States (and, if required by an applicable income tax treaty, are attributable to a United States permanent establishment) are not subject to withholding tax, provided certain certification and disclosure requirements are satisfied. Instead, such dividends are subject to United States federal income tax on a net income basis in the same manner as if the non-U.S. holder were a United States person as defined under the Code. Any such effectively connected dividends received by a foreign corporation may be subject to an additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty.

A non-U.S. holder of our common stock who wishes to claim the benefit of an applicable treaty rate and avoid backup withholding, as discussed below, for dividends will be required (a) to complete IRS Form W-8BEN or IRS Form W-8BEN-E (or other applicable form) and certify under penalty of perjury that such holder is not a United States person as defined under the Code and is eligible for treaty benefits or (b) if the common stock is held through certain foreign intermediaries, to satisfy the relevant certification requirements of applicable Treasury Regulations. Special certification and other requirements apply to certain non-U.S. holders that are pass-through entities rather than corporations or individuals.

A non-U.S. holder of our common stock eligible for a reduced rate of United States withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS.

Gain on disposition of our common stock

Any gain realized on the disposition of our common stock by a non-U.S. holder generally will not be subject to United States federal income tax unless:

the gain is effectively connected with a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, is attributable to a United States permanent establishment of the non-U.S. holder); the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of that disposition, and certain other conditions are met; or we are or have been a United States real property holding corporation for United States federal income tax purposes at any time during the shorter of the five-year period ending on the date of the disposition or such non-U.S. holder's holding period for our common stock and such non-U.S. holder held (at any time during the shorter of the five-year period ending on the date of the disposition or such non-U.S. holder's holding period) more than 5% of our common stock.

An individual non-U.S. holder described in the first bullet point immediately above will be subject to tax on the net gain derived from the sale under regular graduated United States federal income tax rates. If a non-U.S. holder that is a foreign corporation falls under the first bullet point immediately above, it will be subject to tax on its net gain in the same manner as if it were a United States person as defined under the Code and, in addition, may be subject to a branch profits tax equal to 30% of its effectively connected earnings and profits or at such lower rate as may be specified by an applicable income tax treaty.

We believe we have not been and are not currently a United States real property holding corporation for United States federal income tax purposes; however, no assurance can be given that we will not become one in the future. If, however, we are or become a United States real property holding corporation, so long as our common stock continues to be regularly traded on an established securities market, only a non-U.S. holder who holds, or held (at any time during the shorter of the five-year period ending on the date of disposition or the

S-18

TABLE OF CONTENTS

non-U.S. holder's holding period) more than 5% of our common stock will be subject to United States federal income tax on the disposition of the common stock. Non-U.S. holders should consult their own tax advisors about the consequences that could result if we are, or become, a United States real property holding corporation.

Information reporting and backup withholding

We must report annually to the IRS and to each non-U.S. holder the amount of dividends paid to such holder and the tax withheld with respect to such dividends, regardless of whether withholding was required. Copies of the information returns reporting such dividends and withholding may also be made available to the tax authorities in the country in which the non-U.S. holder resides under the provisions of an applicable income tax treaty.

A non-U.S. holder will be subject to backup withholding for dividends paid to such holder unless such holder certifies under penalty of perjury that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that such holder is a United States person as defined under the Code), or such holder otherwise establishes an exemption.

Information reporting and, depending on the circumstances, backup withholding will apply to the proceeds of a sale of our common stock within the United States or conducted through certain United States-related financial intermediaries, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that the beneficial owner is a United States person as defined under the Code), or such owner otherwise establishes an exemption.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's United States federal income tax liability provided the required information is furnished to the IRS.

FATCA withholding requirements

Under Sections 1471 through 1474 of the Code, the Treasury Regulations and official guidance promulgated thereunder and certain intergovernmental agreements entered into between the United States and certain foreign governments (collectively referred to as FATCA), the relevant withholding agent may be required to withhold 30% of any dividends on our common stock, and, beginning in 2017, on the gross proceeds from the sales of our common stock paid to (i) a foreign financial institution unless such foreign financial institution agrees to verify, report and disclose its U.S. accountholders and meets certain other specified requirements (including the local law requirements of a relevant non-U.S. jurisdiction under an applicable intergovernmental agreement) or (ii) a non-financial foreign entity that is the beneficial owner of the payment unless such entity certifies that it does not have any substantial United States owners or provides the name, address and taxpayer identification number of each substantial United States owner and such entity meets certain other specified requirements. Prospective investors are encouraged to consult with their independent tax advisers as to the potential impact of FATCA on their acquisition, ownership and disposition of our common stock based on their particular situations.

TABLE OF CONTENTS

Underwriting

Subject to the terms and conditions set forth in the underwriting agreement, dated March , 2017, between us and Jefferies LLC, as the representative of the underwriters named below and the sole book-running manager of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

Underwriter	Number of Shares
Jefferies LLC	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ per share of common stock. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of \$ per share of common stock to certain brokers and dealers. After the offering, the initial public offering price, concession and reallowance to dealers may be reduced by the representative. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

TABLE OF CONTENTS

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share		Total	
	Without	With	Without	With
	Option	Option to	Option	Option to
	to	Purchase	to	Purchase
	Purchase	Additional	Purchase	Additional
	Additional	Shares	Additional	Shares
	Shares		Shares	
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions paid by us	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$.

Listing

Our common stock is listed on the Nasdaq Capital Market under the trading symbol **TGTX** .

Stamp Taxes

If you purchase shares of common stock offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above.

No Sales of Similar Securities

We and our officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or

publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus without the prior written consent of Jefferies LLC.

This restriction terminates after the close of trading of the common stock on and including the 90th day after the date of this prospectus.

Jefferies LLC may, in its sole discretion and at any time or from time to time before the termination of the 90-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our officers and directors who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

S-21

TABLE OF CONTENTS

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either covered short sales or naked short sales.

Covered short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Naked short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on the Nasdaq Capital Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in

S-22

TABLE OF CONTENTS

any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

S-23

TABLE OF CONTENTS

NOTICE TO INVESTORS

Canada

Resale Restrictions

The distribution of the securities in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the securities in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

Representations of Canadian Purchasers

By purchasing the securities in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

the purchaser is entitled under applicable provincial securities laws to purchase the securities without the benefit of a prospectus qualified under those securities laws as it is an accredited investor as defined under National Instrument 45-106 Prospectus Exemptions, the purchaser is a permitted client as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations, where required by law, the purchaser is purchasing as principal and not as agent, and the purchaser has reviewed the text above under Resale Restrictions.

Conflicts of Interest

Canadian purchasers are hereby notified that Jefferies LLC is relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105 Underwriting Conflicts from having to provide certain conflict of interest disclosure in this document.

Statutory Rights of Action

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the prospectus (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Enforcement of Legal Rights

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a

result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

Taxation and Eligibility for Investment

Canadian purchasers of the securities should consult their own legal and tax advisors with respect to the tax consequences of an investment in the securities in their particular circumstances and about the eligibility of the securities for investment by the purchaser under relevant Canadian legislation.

S-24

TABLE OF CONTENTS

Australia

This prospectus supplement and the accompanying prospectus are not disclosure documents for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, have not been lodged with the Australian Securities & Investments Commission and are only directed to the categories of exempt persons set out below.

Accordingly, if you receive this prospectus supplement in Australia:

You confirm and warrant that you are either a:

sophisticated investor under section 708(8)(a) or (b) of the Corporations Act;
sophisticated investor under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or
professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act, any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date), no offer of any securities which are the subject of the offering contemplated by this prospectus supplement has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;
to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representative of the underwriters for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive;
provided that no such offer of securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus

TABLE OF CONTENTS

Directive means Directive 2003/71/EC (and amendments thereto, including Directive 2010/73/EU, the 2010 PD Amending Directive), and includes any relevant implementing measure in the Relevant Member State.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus supplement and the accompanying prospectus have not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, and any offer of the shares is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and qualified individuals, each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the

laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

S-26

TABLE OF CONTENTS

Singapore

This prospectus supplement and the accompanying prospectus have not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;

where no consideration is given for the transfer; or

where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX) or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

TABLE OF CONTENTS

United Kingdom

This prospectus supplement only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the Order) and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a relevant person).

This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

S-28

TABLE OF CONTENTS

Legal matters

Alston & Bird LLP, New York, New York, has passed upon certain legal matters regarding the shares offered by this prospectus supplement. Covington & Burling, LLP is counsel to the underwriters in connection with this offering.

Experts

The consolidated financial statements of TG Therapeutics, Inc. and subsidiaries as of and for the year ended December 31, 2015 and December 31, 2014 have been incorporated by reference herein in reliance upon the report of CohnReznick LLP, independent registered public accounting firm, and upon the authority of said firm as experts in accounting and auditing.

Where you can find more information

We file annual, quarterly and current reports, proxy statements, and other information with the SEC. You may read and copy any documents we have filed with the SEC at its Public Reference Room located at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. We also file these documents with the SEC electronically. You can access the electronic versions of these filings on the SEC's Internet website found at <http://www.sec.gov>. You can also obtain copies of materials we file with the SEC, free of charge, from our Internet website found at www.tgtherapeutics.com. Information contained on our website does not constitute part of this prospectus supplement or the accompanying prospectus. Our stock is quoted on the Nasdaq Capital Market under the symbol TGTX.

Incorporation of certain information by reference

The SEC allows us to incorporate by reference the information we file with them which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement and accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement and accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus supplement and the termination of the offering (other than, unless otherwise specifically indicated, current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items):

Our Annual Report on Form 10-K for the year ended December 31, 2015;

Our Proxy Statement on Schedule 14A filed with the SEC on April 29, 2016;

Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2016, June 30, 2016, and September 30, 2016; and

Our Current Reports on Form 8-K filed with the SEC on June 2, 2016, June 6, 2016, June 14, 2016, October 13, 2016, December 5, 2016, December 6, 2016, January 4, 2017 and March 6, 2017.

We will provide to each person, including any beneficial owner, to whom a copy of this prospectus supplement and the related prospectus is delivered, a copy of any or all of the information that we have incorporated by reference into this prospectus supplement and the related prospectus, but not delivered with this prospectus supplement and the

related prospectus (see Item 12(c)(1)(i) of Form S-3). We will provide this information upon written or oral request at no cost to the requester. You may request this information by contacting our corporate headquarters at the following address: 2 Gansevoort St., 9th Floor, New York, New York 10014, Attn: Chief Financial Officer, or by calling (212) 554-4484.

S-29

TABLE OF CONTENTS

PROSPECTUS

\$250,000,000

**Common Stock
Preferred Stock
Warrants
Debt Securities
Units**

The following are types of securities that we may offer, issue and sell from time to time, together or separately:

shares of our common stock;
shares of our preferred stock;
warrants;
debt securities; and

units consisting of any combination of our common stock, preferred stock, warrants or debt securities.

We may offer our securities in one or more offerings in amounts, at prices, and on terms determined at the time of the offering. We may sell our securities through agents we select or through underwriters and dealers we select. If we use agents, underwriters or dealers, we will name them and describe their compensation in a prospectus supplement.

This prospectus provides a general description of the securities we may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any securities. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

Our common stock is traded on the Nasdaq Capital Market under the symbol **TGTX**. On December 26, 2014, the per share closing price of our common stock as reported on the Nasdaq Capital Market was \$16.18 per share.

Investing in our securities involves certain risks. See **Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2013, as well as our Quarterly Report on Form 10-Q for the period ended September 30, 2014, which have been filed with the SEC and are incorporated by reference into this prospectus. You should read the entire prospectus carefully before you make your investment decision.**

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is January 21, 2015.

TABLE OF CONTENTS

TABLE OF CONTENTS

Prospectus

	Page
<u>TG THERAPEUTICS, INC.</u>	<u>1</u>
<u>THE OFFERING</u>	<u>2</u>
<u>FORWARD-LOOKING STATEMENTS</u>	<u>3</u>
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	<u>3</u>
<u>IMPORTANT INFORMATION ABOUT THIS PROSPECTUS</u>	<u>3</u>
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	<u>4</u>
<u>RATIO OF EARNINGS/DEFICIENCY TO FIXED CHARGES</u>	<u>5</u>
<u>DESCRIPTION OF CAPITAL STOCK</u>	<u>6</u>
<u>DESCRIPTION OF WARRANTS</u>	<u>7</u>
<u>DESCRIPTION OF DEBT SECURITIES</u>	<u>8</u>
<u>DESCRIPTION OF UNITS</u>	<u>10</u>
<u>PLAN OF DISTRIBUTION</u>	<u>11</u>
<u>LEGAL MATTERS</u>	<u>12</u>
<u>EXPERTS</u>	<u>12</u>

i

TABLE OF CONTENTS

TG THERAPEUTICS, INC.

We are a biopharmaceutical company focused on the acquisition, development and commercialization of novel treatments for cancer and autoimmune diseases. We acquire rights to these technologies by licensing or otherwise acquiring an ownership interest, funding their research and development, and eventually either out-licensing or bringing the technologies to market. Currently, we are developing two therapies targeting hematological malignancies:

TG-1101 (ublituximab) a novel, glycoengineered monoclonal antibody that targets a specific and unique epitope on the CD20 antigen found on mature B-lymphocytes; and

TGR-1202, an orally available PI3K delta inhibitor.

We are also developing a portfolio of inhibitors of IRAK-4 (interleukin-1 receptor-associated kinase 4), which is currently in pre-clinical development.

We also actively evaluate complementary products, technologies and companies for in-licensing, partnership, acquisition and/or investment opportunities. To date, we have not received approval for the sale of any of our drug candidates in any market and, therefore, have not generated any product sales from our drug candidates.

Our principal executive offices are located at 3 Columbus Circle, New York, New York 10019, and our telephone number is 212-554-4484. We maintain a website on the Internet at *www.tgtherapeutics.com* and our e-mail address is *info@tgtxinc.com*. Our Internet website, and the information contained on it, are not to be considered part of this prospectus.

TABLE OF CONTENTS

THE OFFERING

Use of Proceeds

We intend to use the net proceeds of any offering as set forth in the applicable prospectus supplement.

Nasdaq Symbol

TGTX

2

TABLE OF CONTENTS

FORWARD-LOOKING STATEMENTS

This prospectus includes statements that are, or may be deemed, forward-looking statements. In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms believes, estimates, anticipates, expects, plans, intends, may, could, might, will, should, approximately negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. They appear in a number of places throughout this prospectus (and the documents incorporated by reference into this prospectus) and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned discovery and development of drugs targeting cancer, the strength and breadth of our intellectual property, our ongoing and planned preclinical studies and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, the degree of clinical utility of our product candidates, particularly in specific patient populations, expectations regarding clinical trial data, our results of operations, financial condition, liquidity, prospects, growth and strategies, the length of time that we will be able to continue to fund our operating expenses and capital expenditures, our expected financing needs and sources of financing, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus (and the documents incorporated by reference into this prospectus), we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this prospectus. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this prospectus (and the documents incorporated by reference into this prospectus), they may not be predictive of results or developments in future periods.

WHERE YOU CAN FIND MORE INFORMATION

We file reports with the SEC on an annual basis using Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K. You may read and copy any such reports and amendments thereto at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 on official business days during the hours of 10:00 a.m. to 3:00 p.m.

Please call the SEC at 1-800-SEC-0330 for information on the Public Reference Room. Additionally, the SEC maintains a website that contains annual, quarterly, and current reports, proxy statements, and other information that issuers (including us) file electronically with the SEC. The SEC's website address is <http://www.sec.gov>. You can also obtain copies of materials we file with the SEC from our Internet website found at www.tgtherapeutics.com. Our stock is quoted on the Nasdaq Capital Market under the symbol TGTX.

IMPORTANT INFORMATION ABOUT THIS PROSPECTUS

This prospectus is part of a shelf registration statement that we filed with the SEC. By using a shelf registration

statement, we may sell our securities, as described in this prospectus, from time to time in one or more offerings. We may use the shelf registration statement to offer and sell securities described in this prospectus. Each time we sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the terms of such offering. The supplement may also add, update or change information contained in this prospectus. Before purchasing any securities, you should carefully read both this prospectus and any supplement, together with the additional information incorporated into this prospectus or described under the heading **Where You Can Find More Information**.

You should rely only on the information contained or incorporated by reference in this prospectus and any prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We

TABLE OF CONTENTS

will not make an offer to sell securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, as well as information we previously filed with the SEC and have incorporated by reference, is accurate as of the date on the front cover of this prospectus only, or when such document was filed with the SEC. Our business, financial condition, results of operations and prospects may have changed since the relevant date.

We will not use this prospectus to offer and sell securities unless it is accompanied by a prospectus supplement that more fully describes the terms of the offering.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information we file with the SEC. This means that we can disclose important information to you by referring you to those documents without restating that information in this document. The information incorporated by reference into this prospectus is considered to be part of this prospectus, and information we file with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, after the date of this prospectus and prior to the termination of this offering, will automatically update and supersede the information contained in this prospectus and documents listed below. We incorporate by reference into this prospectus the documents listed below, except to the extent information in those documents differs from information contained in this prospectus, and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including exhibits:

- (a) Our Annual Report on Form 10-K for the year ended December 31, 2013;
- (b) Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014, June 30, 2014 and September 30, 2014;
- (c) Our Current Reports on Form 8-K filed with the SEC on March 6, 2014, March 12, 2014, March 17, 2014, May 12, 2014, May 30, 2014, June 10, 2014, June 12, 2014, June 13, 2014, June 27, 2014, July 21, 2014, September 15, 2014, September 23, 2014, November 10, 2014, November 14, 2014, December 9, 2014 and December 17, 2014;
- (d) Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 23, 2014; and
- (e) The description of our common stock contained in our registration statement on Form 8-A filed with the SEC on May 28, 2013 (File No. 001-32639).

We will provide to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of any or all of the information that we have incorporated by reference into this prospectus. We will provide this information upon written or oral request at no cost to the requester. You may request this information by contacting our corporate headquarters at the following address: 3 Columbus Circle, 15th Floor, New York, New York 10019, Attn: Chief Financial Officer, or by calling (212) 554-4484.

TABLE OF CONTENTS**RATIO OF EARNINGS/DEFICIENCY TO FIXED CHARGES**

The following table sets forth, for each of the periods presented, our ratio of earnings to fixed charges and our coverage deficiency. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

(in thousands)	Nine Months Ended September 30, 2014	Year Ended December 31, 2013	Year Ended December 31, 2012	Year Ended December 31, 2011
Net loss	36,985	20,478	26,183	889
Ratio of earnings to fixed charges ⁽¹⁾	N/A	N/A	N/A	N/A
Coverage deficiency	(36,985)	(20,478)	(26,183)	(889)

We did not record earnings for the nine months ended September 30, 2014, and for the years ended December 31, (1)2013, 2012 and 2011. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods.

5

TABLE OF CONTENTS

DESCRIPTION OF CAPITAL STOCK

The following summary of the terms of our capital stock may not be complete and is subject to, and qualified in its entirety by reference to, the terms and provisions of our amended and restated certificate of incorporation and our restated bylaws. You should refer to, and read this summary together with, our amended and restated certificate of incorporation and restated bylaws to review all of the terms of our capital stock that may be important to you.

Common Stock

Under our certificate of incorporation, we are authorized to issue a total of 150,000,000 shares of common stock, par value \$0.001 per share. As of November 13, 2014 we had issued and outstanding 43,964,350 shares of our common stock. There are approximately 476 holders of record. All outstanding shares of our common stock are fully paid and nonassessable. Our common stock is listed on the Nasdaq Capital Market under the symbol TGTX.

Dividends

Subject to the dividend rights of the holders of any outstanding series of preferred stock, holders of our common stock are entitled to receive ratably such dividends and other distributions of cash or any other right or property as may be declared by our board of directors out of our assets or funds legally available for such dividends or distributions.

Voting Rights

The holders of our common stock are entitled to one vote for each share of common stock owned by that stockholder on every matter properly submitted to the stockholders for their vote. Stockholders are not entitled to vote cumulatively for the election of directors.

Liquidation and Dissolution

In the event of any voluntary or involuntary liquidation, dissolution or winding up of our affairs, holders of common stock would be entitled to share ratably in our assets that are legally available for distribution to stockholders after payment of liabilities. If we have any preferred stock outstanding at such time, holders of the preferred stock may be entitled to distributions and/or liquidation preferences. In either such case, we must pay the applicable distribution to the holders of our preferred stock (if any) before we may pay distributions to the holders of common stock.

Other

Holders of our common stock have no conversion, redemption, preemptive, subscription or similar rights.

Transfer Agent

American Stock Transfer and Trust Company serves as the transfer agent and registrar for all of our common stock.

Preferred Stock

Under the terms of our restated certificate of incorporation, our board of directors is authorized to issue up to 10,000,000 shares of preferred stock, par value \$0.001 per share. Our board of directors may issues shares of preferred

stock in one or more series without stockholder approval, and has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. We may amend from time to time our restated certificate of incorporation to increase the number of authorized shares of preferred stock. Any such amendment would require the approval of the holders of a majority of the voting power of the shares entitled to vote thereon. As of the date of this prospectus, we have 10,000,000 shares of preferred shares authorized, but no shares of preferred stock outstanding.

It is not possible to state the actual effect of the issuance of any shares of preferred stock upon the rights of the holders of common stock until the board of directors determines the specific rights of the holders of preferred stock. However, effects of the issuance of preferred stock include restricting dividends on common

TABLE OF CONTENTS

stock, diluting the voting power of common stock, impairing the liquidation rights of common stock, and making it more difficult for a third party to acquire us, which could have the effect of discouraging a third party from acquiring, or deterring a third party from paying a premium to acquire, a majority of our outstanding voting stock.

The particular terms of any series of preferred stock being offered by us will be described in the prospectus supplement relating to that series of preferred stock. Those terms may include:

- the title and liquidation preference per share of the preferred stock and the number of shares offered;
- the purchase price of the preferred stock;
- the dividend rate (or method of calculation);
- the dates on which dividends will be paid and the date from which dividends will begin to accumulate;
- any redemption or sinking fund provisions of the preferred stock;
- any listing of the preferred stock on any securities exchange or market;
- any conversion provisions of the preferred stock;
- the voting rights, if any, of the preferred stock; and
- any additional dividend, liquidation, redemption, sinking fund and other rights, preferences, privileges, limitations and restrictions of the preferred stock.

The preferred stock will, when issued, be fully paid and non-assessable.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase shares of our common stock and/or preferred stock in one or more series together with other securities or separately, as described in each applicable prospectus supplement.

The prospectus supplement relating to any warrants we offer will include specific terms relating to the offering. These terms will include some or all of the following:

- the title of the warrants;
- the aggregate number of warrants offered;
- the designation, number and terms of the shares of common stock purchasable upon exercise of the warrants and procedures by which those numbers may be adjusted;
- the exercise price of the warrants;
- the dates or periods during which the warrants are exercisable;
- the designation and terms of any securities with which the warrants are issued;
- if the warrants are issued as a unit with another security, the date on and after which the warrants and the other security will be separately transferable;
- if the exercise price is not payable in U.S. dollars, the foreign currency, currency unit or composite currency in which the exercise price is denominated;
- any minimum or maximum amount of warrants that may be exercised at any one time;
- any terms relating to the modification of the warrants;
- any terms, procedures and limitations relating to the transferability, exchange or exercise of the warrants; and
- any other specific terms of the warrants.

TABLE OF CONTENTS

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior, subordinated or junior subordinated and may be convertible. Unless otherwise specified in the applicable prospectus supplement, our debt securities will be issued in one or more series under an indenture to be entered into between us and a trustee. We will issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

The following description briefly sets forth certain general terms and provisions of the debt securities that we may offer. The particular terms of the debt securities offered by any prospectus supplement and the extent, if any, to which these general provisions may apply to the debt securities, will be described in the related prospectus supplement. Accordingly, for a description of the terms of a particular issue of debt securities, reference must be made to both the related prospectus supplement and to the following description.

Debt Securities

The aggregate principal amount of debt securities that may be issued under the indenture is unlimited. The debt securities may be issued in one or more series as may be authorized from time to time pursuant to a supplemental indenture entered into between us and the trustee or an order delivered by us to the trustee. For each series of debt securities we offer, a prospectus supplement accompanying this prospectus will describe the following terms and conditions of the series of debt securities that we are offering, to the extent applicable:

- title and aggregate principal amount;
- whether the debt securities will be senior, subordinated or junior subordinated;
- applicable subordination provisions, if any;
- provisions regarding whether the debt securities will be convertible or exchangeable into other securities or property of the Company or any other person;
- percentage or percentages of principal amount at which the debt securities will be issued;
- maturity date(s);
- interest rate(s) or the method for determining the interest rate(s);
- whether interest on the debt securities will be payable in cash or additional debt securities of the same series;
- dates on which interest will accrue or the method for determining dates on which interest will accrue and dates on which interest will be payable;
- whether the amount of payment of principal of, premium, if any, or interest on the debt securities may be determined with reference to an index, formula or other method;
- redemption, repurchase or early repayment provisions, including our obligation or right to redeem, purchase or repay debt securities under a sinking fund, amortization or analogous provision;
- if other than the debt securities principal amount, the portion of the principal amount of the debt securities that will be payable upon declaration of acceleration of the maturity;
- authorized denominations;
- form;
- amount of discount or premium, if any, with which the debt securities will be issued, including whether the debt

securities will be issued as original issue discount securities;

8

TABLE OF CONTENTS

the place or places where the principal of, premium, if any, and interest on the debt securities will be payable;
where the debt securities may be presented for registration of transfer, exchange or conversion;
the place or places where notices and demands to or upon the Company in respect of the debt securities may be made;
whether the debt securities will be issued in whole or in part in the form of one or more global securities;
if the debt securities will be issued in whole or in part in the form of a book-entry security, the depository or its nominee with respect to the debt securities and the circumstances under which the book-entry security may be registered for transfer or exchange or authenticated and delivered in the name of a person other than the depository or its nominee;
whether a temporary security is to be issued with respect to such series and whether any interest payable prior to the issuance of definitive securities of the series will be credited to the account of the persons entitled thereto;
the terms upon which beneficial interests in a temporary global security may be exchanged in whole or in part for beneficial interests in a definitive global security or for individual definitive securities;
the guarantors, if any, of the debt securities, and the extent of the guarantees and any additions or changes to permit or facilitate guarantees of such debt securities;
any covenants applicable to the particular debt securities being issued;
any defaults and events of default applicable to the debt securities, including the remedies available in connection therewith;
currency, currencies or currency units in which the purchase price for, the principal of and any premium and any interest on, such debt securities will be payable;
time period within which, the manner in which and the terms and conditions upon which the Company or the purchaser of the debt securities can select the payment currency;
securities exchange(s) on which the debt securities will be listed, if any;
whether any underwriter(s) will act as market maker(s) for the debt securities;
extent to which a secondary market for the debt securities is expected to develop;
provisions relating to defeasance;
provisions relating to satisfaction and discharge of the indenture;
any restrictions or conditions on the transferability of the debt securities;
provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
any addition or change in the provisions related to compensation and reimbursement of the trustee;
provisions, if any, granting special rights to holders upon the occurrence of specified events;
whether the debt securities will be secured or unsecured, and, if secured, the terms upon which the debt securities will be secured and any other additions or changes relating to such security; and
any other terms of the debt securities that are not inconsistent with the provisions of the Trust Indenture Act (but may modify, amend, supplement or delete any of the terms of the indenture with respect to such series of debt securities).

9

TABLE OF CONTENTS

General

One or more series of debt securities may be sold as original issue discount securities. These debt securities would be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at the time of issuance is below market rates. One or more series of debt securities may be variable rate debt securities that may be exchanged for fixed rate debt securities.

United States federal income tax consequences and special considerations, if any, applicable to any such series will be described in the applicable prospectus supplement.

Debt securities may be issued where the amount of principal and/or interest payable is determined by reference to one or more currency exchange rates, commodity prices, equity indices or other factors. Holders of such debt securities may receive a principal amount or a payment of interest that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending upon the value of the applicable currencies, commodities, equity indices or other factors. Information as to the methods for determining the amount of principal or interest, if any, payable on any date, the currencies, commodities, equity indices or other factors to which the amount payable on such date is linked and certain additional United States federal income tax considerations will be set forth in the applicable prospectus supplement.

The term debt securities includes debt securities denominated in U.S. dollars or, if specified in the applicable prospectus supplement, in any other freely transferable currency or units based on or relating to foreign currencies.

We expect most debt securities to be issued in fully registered form without coupons and in denominations of \$2,000 and any integral multiples thereof. Subject to the limitations provided in the indenture and in the prospectus supplement, debt securities that are issued in registered form may be transferred or exchanged at the principal corporate trust office of the trustee, without the payment of any service charge, other than any tax or other governmental charge payable in connection therewith.

Global Securities

The debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with, or on behalf of, a depository identified in the prospectus supplement. Global securities will be issued in registered form and in either temporary or definitive form. Unless and until it is exchanged in whole or in part for the individual debt securities, a global security may not be transferred except as a whole by the depository for such global security to a nominee of such depository or by a nominee of such depository to such depository or another nominee of such depository or by such depository or any such nominee to a successor of such depository or a nominee of such successor. The specific terms of the depository arrangement with respect to any debt securities of a series and the rights of and limitations upon owners of beneficial interests in a global security will be described in the applicable prospectus supplement.

Governing Law

The indenture and the debt securities shall be construed in accordance with and governed by the laws of the State of New York.

DESCRIPTION OF UNITS

We may issue, in one more series, units comprised of shares of our common stock or preferred stock, warrants to purchase common stock or preferred stock, debt securities or any combination of those securities. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We may evidence units by unit certificates that we issue under a separate agreement. We may issue the units under a unit agreement between us and one or more unit agents. If we elect to enter into a unit agreement with a unit agent, the unit agent will act solely as our agent in connection with the units and will not assume any obligation or relationship of agency or trust for or with any registered holders of units or

TABLE OF CONTENTS

beneficial owners of units. We will indicate the name and address and other information regarding the unit agent in the applicable prospectus supplement relating to a particular series of units if we elect to use a unit agent.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions of the governing unit agreement that differ from those described herein; and
any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The other provisions regarding our common stock, preferred stock, warrants and debt securities as described in this section will apply to each unit to the extent such unit consists of shares of our common stock, preferred stock, warrants and/or debt securities.

PLAN OF DISTRIBUTION

We may sell the securities covered in this prospectus in any of three ways (or in any combination):

through underwriters or dealers;
directly to a limited number of purchasers or to a single purchaser; or
through agents.

Each time that we use this prospectus to sell securities, we will also provide a prospectus supplement that contains the specific terms of the offering. The prospectus supplement will set forth the terms of the offering of the securities, including:

the name or names of any underwriters, dealers or agents and the amounts of any securities underwritten or purchased by each of them; and

the public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers.

Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

If underwriters are used in the sale of any securities, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase the securities will be subject to certain conditions precedent. The underwriters will be obligated to purchase all of the securities if they purchase any of securities.

We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for

solicitation of these contracts.

Agents and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act of 1933, as amended, or to contribution with respect to payments

TABLE OF CONTENTS

which the agents or underwriters may be required to make in respect thereof. Agents and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of securities, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of securities. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment).

In compliance with the guidelines of the Financial Services Regulatory Authority, Inc., or FINRA, the maximum compensation to be received by a FINRA member or independent broker-dealer may not exceed 8% of the offering proceeds. It is anticipated that the maximum compensation to be received in any particular offering of securities will be less than this amount.

LEGAL MATTERS

The legality and validity of the securities offered from time to time under this prospectus will be passed upon by Alston & Bird LLP, New York, New York.

EXPERTS

The consolidated financial statements of TG Therapeutics, Inc. and Subsidiaries as of December 31, 2013 and 2012, and for the years then ended, and the cumulative period ended December 31, 2013, have been incorporated by reference herein and in the registration statement in reliance upon the report of CohnReznick LLP, independent registered public accounting firm, and upon the authority of said firm as experts in accounting and auditing.

TABLE OF CONTENTS

shares

Common Stock

Prospectus Supplement

Jefferies

, 2017