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**Recent Events: Special Protocol Assessment (SPA) agreement reached with FDA for Phase 3 registration trial of TG-1101 in combination with ibrutinib for patients with previously treated Chronic Lymphocytic Leukemia; key data on two programs is expected to be released this December at ASH; initiated first clinical trial evaluating 'all oral' combination of TGR-1202 and ibrutinib.**

### KEY CONSIDERATIONS

- TG Therapeutics' lead candidate TG-1101 first registration program is in combination with ibrutinib for previously treated Chronic Lymphocytic Leukemia (CLL) patients.
- TG-1101 is a glyco-engineered (enhanced) version of Rituxan, the \$7 billion a year (sales) leading therapy for Non-Hodgkin's Lymphoma (NHL) and many other B-cell mediated diseases, including CLL.
- Multiple preclinical and clinical studies have shown TG-1101 alone and in combination is superior to Rituxan in B-cell killing power.
- In September 2014, TG Therapeutics announced an agreement with the FDA for a Special Protocol Assessment (SPA) on the design, end points and statistical analysis of a Phase 3 registration trial of TG-1011 in combination with ibrutinib, providing a clear path forward for the Company's first candidate. A 330-patient trial in CLL under the SPA is expected to initiate in 4Q 2014.
- If the Phase 3 program is successful, TG-1101 would be the first anti-CD20 antibody approved in combination with ibrutinib.
- An open label Phase 2 clinical trial with this same combination therapy recently completed enrollment and top line data on more than 30 patients is expected to be presented in December at the American Society of Hematology (ASH) in San Francisco.
- Approximately 85,000 men and women in the U.S. are diagnosed with NHL and CLL each year and most will eventually fail Rituxan therapy if they aren't initially resistant.
- In September 2014, TG Therapeutics exercised an option for an exclusive worldwide license (ex. India) for its second B-cell-killing candidate, TGR-1202, a novel orally-dosed kinase inhibitor.
- TGR-1202 belongs to the PI3K class of kinase inhibitors, known potent disrupters of B-cell activity; Gilead (GILD) recently

### TG Therapeutics, Inc. (TGTX)

Recent Price:	\$14.50
Shares Outstanding:	44 million
Approx. MktCap:	\$638 million
Fiscal Year Ends:	Dec. 31
Cash (9/30/14-pro forma):	\$93.4 million
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received FDA approval for idelalisib, the first of the class to be approved for B-cell malignancies.

•TGR-1202 has demonstrated impressive clinical activity as a single agent and is now being successfully tested in combination with TG-1011 in patients with especially aggressive CLL and NHL with new data expected to be ready for presentation at the December 2014 ASH meeting.

•Hepatotoxicity and GI toxicity have been prevalent in the other PI3K deltas in development, and resulted in a black-box warning label for Gilead's idelalisib. TGR-1202 has been devoid of these toxicities to date.

•Infinity Pharmaceuticals (INFI) recently entered into a global collaboration with AbbVie Pharmaceuticals (ABBV) to develop IPI-145, another PI3K inhibitor. Total deal value was more than \$800 million with \$275 million received upfront.

### OVERVIEW

TG Therapeutics is led by Executive Chairman and Interim CEO Michael S. Weiss, who was formerly Chairman/CEO of Keryx Biopharmaceuticals which has grown into a \$1.3 billion market cap Nasdaq-traded company. Under his leadership, Keryx negotiated six Special Protocol Assessments (SPAs) with the FDA and launched six Phase 3 clinical trials, with a total of more than 4,000 patients, for treatments of oncology and renal conditions. Mr. Weiss was also the founder of ACCESS Oncology.

TGTX is developing two drug candidates, both engineered for effectiveness against "B-cell proliferative" diseases which include lymphomas, leukemia, and autoimmune disorders.

### TG-1101

TG-1101 borrows a page from the classical effectiveness of Rituxan, a gold standard treatment for NHL and CLL and many other B-cell mediated diseases.

Like Rituxan, TG-1101 is a monoclonal antibody that targets the CD20 antigen. Anti-CD20 antibodies operate by killing malignant B-cells.

But the similarity ends there. TG-1101 attaches to a different location on the CD20 antigen, which means patients who have developed resistance to Rituxan may still respond to TG-1101. Additionally it has been bioengineered to induce a greater immune response, which gives it much more potent killing power.

To develop the optimal therapeutic benefit from TG-1101, the Company teamed it with ibrutinib (IMBRUVICA™), a BTK inhibitor from Pharmacocyclics/Janssen in a Phase 2 study to assess Overall Response Rate (ORR) in relapsed or refractory patients with CLL and Mantle Cell Lymphoma (MCL), a particularly aggressive form of NHL.

The initial efficacy assessment (10 of the 28 patients) (reported on June 13, 2014 at the 19th Annual European Hematology Association [EHA] in Milan), showed the combination therapy produced a 90 percent ORR.

These significant and very promising early results led to a September 2014 Special Protocol Agreement (SPA) with the FDA for a Phase 3 registration trial with ORR as the primary endpoint to support accelerated approval and progression-free survival to support full marketing approval. The Company expects to launch the 330-patient trial in 4Q 2014.

The poster presentation at the EHA included data from 28 patients with relapsed and/or refractory CLL or MCL treated with TG-1101 at doses of 600 mg or 900 mg in combination with ibrutinib at an oral daily dose of 420 mg for patients with CLL and 560 mg for patients with MCL.

The breakdown of the 90 percent ORR for the 10 evaluable patients is as follows:

•CLL patients (including 4 with high risk cytogenetics): 86% (6/7) achieved a partial response (PR) at the first assessment, with the remaining one patient achieving a 40%

nodal reduction coupled with a > 50% reduction in ALC pending next response assessment; and

• MCL patients: 100% (3/3) achieved a response (1 CR and 2 PRs).

TG-1101 in combination with ibrutinib was well tolerated in the 28 patients evaluable for safety, with Day 1 infusion related reactions (IRR) being the most frequently reported adverse event for TG-1101. All but one IRR were Grade 1 or 2 in severity and were manageable without dose reductions. Ibrutinib related adverse events included diarrhea and rash with one patient discontinuing treatment due to ibrutinib related diarrhea (only patient to discontinue from the study to date).

The addition of TG-1101 appears to eliminate ibrutinib related lymphocytosis in patients with CLL, with patients experiencing a median ~80 percent reduction in their absolute lymphocyte count (ALC) by month 4 following initiation of combination therapy.

TG Therapeutics acquired exclusive worldwide rights (excluding France and Belgium) to TG-1101 in January 2012 from LFB Biotechnologies S.A.S., a 1500-employee French pharmaceuticals firm wholly owned by the French government.

The Company will pay LFB achievement milestones and single digit royalties.

TG Therapeutics subsequently licensed exclusive rights to develop and commercialize TG-1101 in South Korea and Southeast Asia to Ildong Pharmaceutical Co., Ltd. in exchange for \$2 million upfront and sales-based milestones and royalty payments.

### TGR-1202

TGR-1202 belongs to the same class of kinase inhibitors (PI3K delta) as the kinase inhibitor Gilead acquired in a \$600 million (including milestones) deal with Calistoga in 2011. The Calistoga program was in Phase 2 at the time Gilead acquired it.

TGR-1202 is an orally-dosed small molecule designed to disrupt a vastly different mechanism than the IV-dosed TG-1101 antibody. As such, TGR-1202 broadens the Company's ability to produce medicines effective against the broad range of B-cell mediated diseases, and, in fact, to study the potential benefits of combining TG-1101 and TGR-1202 in treating particularly aggressive forms of B-cell mediated cancers.

The initial clinical data on combination TG-1011 and TGR-1202 therapy was first presented last July at the 2014 Pan Pacific Lymphoma Conference.

The Phase 1 dose-escalating study showed that in previously treated patients with high-risk CLL and other aggressive lymphomas, the combination of TG-1101 and TGR-1202 produced a significant nodal reduction in 100 percent of the patients with either a normalization of or roughly 80 reduction in Blood Lymphocyte Count. Four of five of the patients achieved a partial response at first assessment, including a patient relapsed from

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a prior BTK-inhibitor, and the 5th patient with stable disease achieved a 44 percent nodal reduction pending next assessment.

Similarly positive early results were reported for 10 heavily pre-treated evaluable patients with non-Hodgkin's Lymphoma, or NHL. The investigators concluded the combination of TG-1011 and TGR-1202 appears well tolerated with no dose-related increases in toxicity observed to date.

Earlier studies with single agent TGR-1202 support its clean toxicity profile. In data presented at the May 2014 ASCO meeting (scheduled for updating at the December 2014 ASH meeting) TGR-1202 demonstrated best-in class activity against three cancers (CLL and two types of NHL) with no dose-related trends in adverse events up through 800 mgs, with higher doses planned.

In December 2014, TG Therapeutics initiated the first 'all oral' combination Phase 1 study of TGR-1202 and ibrutinib in relapsed and refractory CLL and MCL patients in collaboration with the Blood Cancer Research Partnership and Dana-Farber Cancer Institute.

In September 2014, based on safety and efficacy seen to date, the Company exercised its option to license global rights to TGR-1202 from Rhizen Pharmaceuticals, S A ("Rhizen"). The Company and Rhizen have to date been jointly developing TGR-1202 in a 50:50 joint venture. Given the successful development of TGR-1202, TG Therapeutics elected an early exercise of the Company's license option.

The agreement also provides for Rhizen

to contribute backup molecules, giving TG Therapeutics multiple opportunities to develop differentiated therapies against hematologic cancers and autoimmune diseases.

### NHL/CLL MARKETS

Rituxan was approved by the FDA in 1997 as the first anti-CD20 monoclonal antibody. It quickly became the gold standard of treatment for NHL and CLL. With an annual per patient treatment cost of approximately \$50,000, Rituxan now has worldwide sales of \$7 billion.

In the U.S. alone, approximately 70,000 men and women are diagnosed with NHL each year. Almost 19,000 die from the disease. Similarly, 16,000 new cases of CLL are reported annually with almost 5,000 deaths.

Rituxan is effective when used alone as a monotherapy for approximately one-half of all patients. When combined with the "R-CHOP" regimen of chemotherapy, it's effective for approximately 80 percent of patients. (R-CHOP consists of four drugs: cyclophosphamide, doxorubicin, vincristine, and prednisolone.)

A number of patients do not respond to Rituxan at all. Others develop resistance to the drug during the course of multiple treatments which are required as the result of frequent relapses.

With the known failure rate of Rituxan in NHL and CLL patients and anticipated pricing comparable to Rituxan (in the \$50,000 range), the suggested market opportunity for TG Therapeutics' first two candidates could approach or exceed \$2 billion annually.

### SUMMARY POINTS

- **TG Therapeutics is developing improved versions of two drug agents designed to disrupt aberrant B-cell activity, the cause of many cancers and autoimmune diseases.**
- **One, TG-1101, is a novel anti-CD20 antibody, a more powerful version of Rituxan®; the other, TGR-1202, is an oral kinase inhibitor that disrupts B-cell activity in a wholly different way than antibody therapy.**
- **Both candidates are being developed as combination therapies as alternative and/or second line treatments for patients who are not responsive to existing therapies.**
- **The Company expects to initiate enrollment in a 330-patient Phase 3 registration trial of TG-1011 in combination with ibrutinib in CLL patients in 4Q 2014 under a SPA agreement with the FDA announced in September 2014. Primary endpoint for accelerated approval is Overall Response Rate.**
- **Data from a completed Phase 2 study of TG-1011 in combination with ibrutinib is planned for presentation this December at the ASH annual meeting in San Francisco.**
- **Additional data from on-going Phase 1 studies of TG-1011 in combination with TGR-1202 and single agent TGR-1202 is also scheduled for presentation at the upcoming ASH meeting.**
- **The initial target markets for the Company's current candidates have potential sales greater than \$1 billion annually.**
- **TG Therapeutics is well funded with approximately \$93.4 million in cash/equivalents (*pro forma*) at September 30, 2014.**