



# TG Therapeutics

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**NASDAQ: TGTX**

January 2014

# Forward Looking Safe Harbor Statement



*This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are often, but not always, made through the use of words or phrases such as “anticipates”, “expects”, “plans”, “believes”, “intends”, and similar words or phrases. Such statements involve risks and uncertainties that could cause TG Therapeutics’ actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in clinical trials, drug development, and commercialization. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement and TG Therapeutics undertakes no obligation to update these statements, except as required by law.*

- Emerging biopharmaceutical company focused on cancer & autoimmune-related diseases
- Developing two drugs for B-cell cancers – Leukemia and Lymphoma
  - **TG-1101** – Novel Glycoengineered, Anti-CD20 monoclonal antibody
    - Same class as Rituxan<sup>®</sup>, which has ~\$7BB WW Sales
    - Enhanced ADCC profile for increased potency similar to Gazyva<sup>®</sup> (GA101)
    - Single agent activity demonstrated in CLL and NHL in Phase 1/2 studies
  - **TGR-1202** – Novel PI3K $\delta$  inhibitor
    - Same class as Idelalisib and IPI-145
    - Currently in Phase 1 dose escalation study & combination study w/ TG-1101
    - Potential for best in class attributes

# Treatment of B-cell cancers

## Evolving market dynamics



***Treatment of B-cell malignancies could exceed \$10-\$15B***

***Evolving landscape...***

Glyco-engineered CD20s	BTK inhibitors	Delta inhibitors	Bcl-2 inhibitors
Gazyva	Ibrutinib	Idelalisib	Abt-199
TG-1101	CELG	IPI-145	
	Ono	TGR-1202	

***Goal...non-chemotherapy-based combinations, with:***

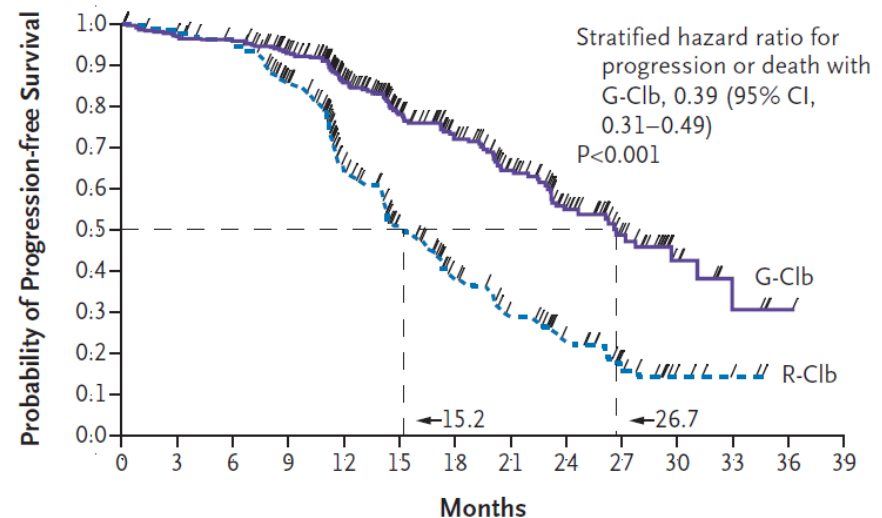
- Anti-CD20's continuing to be the backbone; and
- Novel kinase inhibitors
  - BTK inhibitors;
  - PI3K Delta inhibitors; and/or
  - Bcl-2 inhibitors

- TG-1101 Profile:
  - Novel protein sequence
  - Targets distinct epitope on CD20
  - Glycoengineered for enhanced activity
  - Demonstrated Single Agent activity in relapsed/refractory NHL & CLL

## Proof of Principle for Glycoengineering

- Lower fucose content enhances ADCC, which in turn increases cell killing potency
- TG-1101 has 50-100x the ADCC effects of Rituxan
- Believed to be comparable to GA101

### Ph III: GA101 vs. RTX

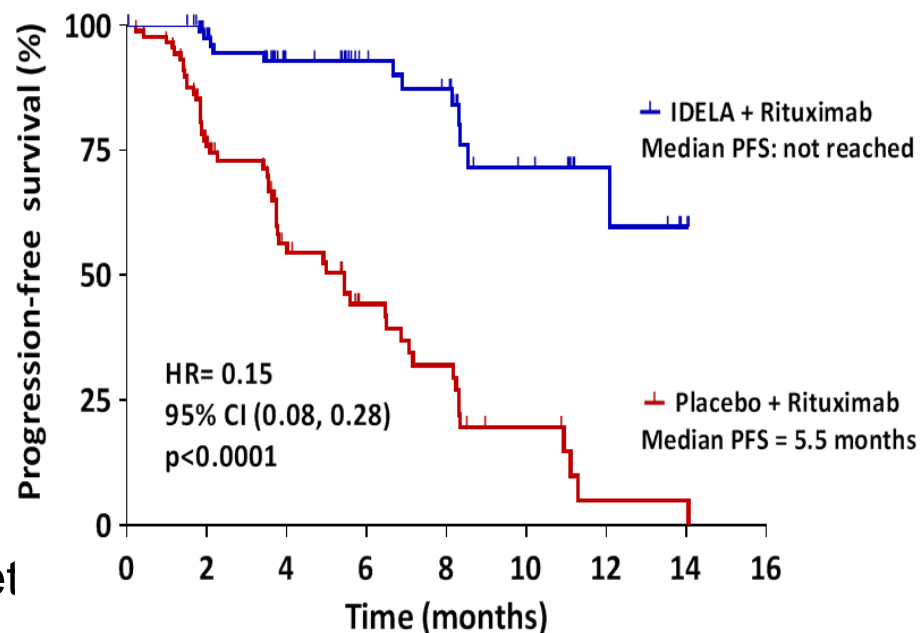


# TGR-1202, a novel PI3k-Delta inhibitor with best in class attributes



- TGR-1202 Profile:
  - Highly selective for Delta with low nanomolar potency
  - Pre-clinical activity profile similar to Idelalisib
  - Designed to avoid liver tox
  - Best in class PK profile
  - Tox profile supports multi-drug combinations
- Best-in-class attributes:
  - Once per day dosing
  - Prolonged half-life maintains target exposure over 24hour period
  - Low incidence of GI toxicity
  - No drug related hepatotoxicity seen to date

## CD20 + PI3K-Delta Proof of Concept: Idelalisib + RTX vs. RTX



# Development Update



- Completed enrollment into TG-1101 Phase I Study in NHL (n=12) and Expansion cohorts in NHL and CLL (n=20).
- Phase I study of TGR-1202 now in 7<sup>th</sup> Cohort (1800 mg)
  - 26 patients enrolled to date
  - PI3K Delta activity confirmed with 3 of 4 CLL patients at 800mg demonstrating nodal PR
  - Opened first expansion cohort for TGR-1202 (800 mg)
- Commenced combination clinical program:
  - TG-1101 (glycoengineered CD20) in combination ibrutinib (BTK inhibitor)
  - TG-1101 (glycoengineered CD20) in combination with TGR-1202 (Delta inhibitor)

# COMBINATION CLINICAL PROGRAM

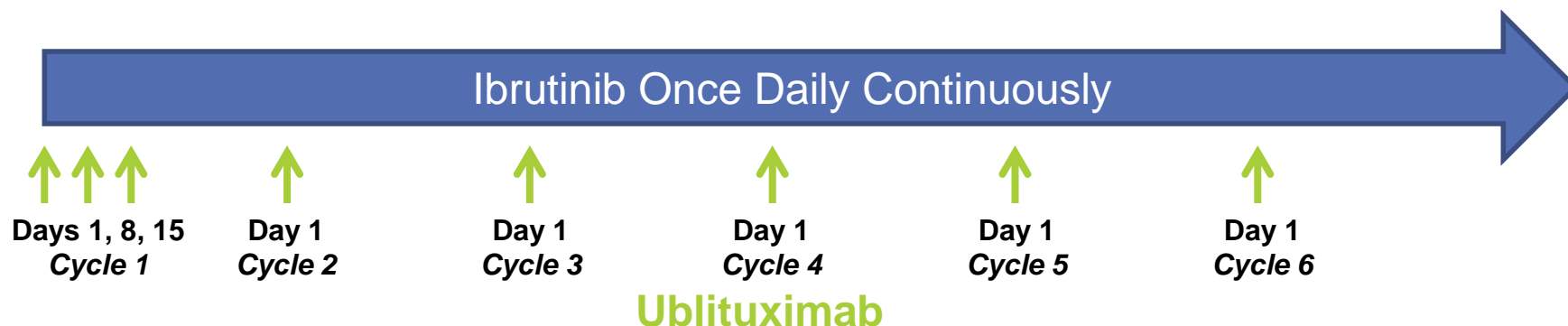
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TG Therapeutics



# Phase II Study of TG-1101 + Ibrutinib

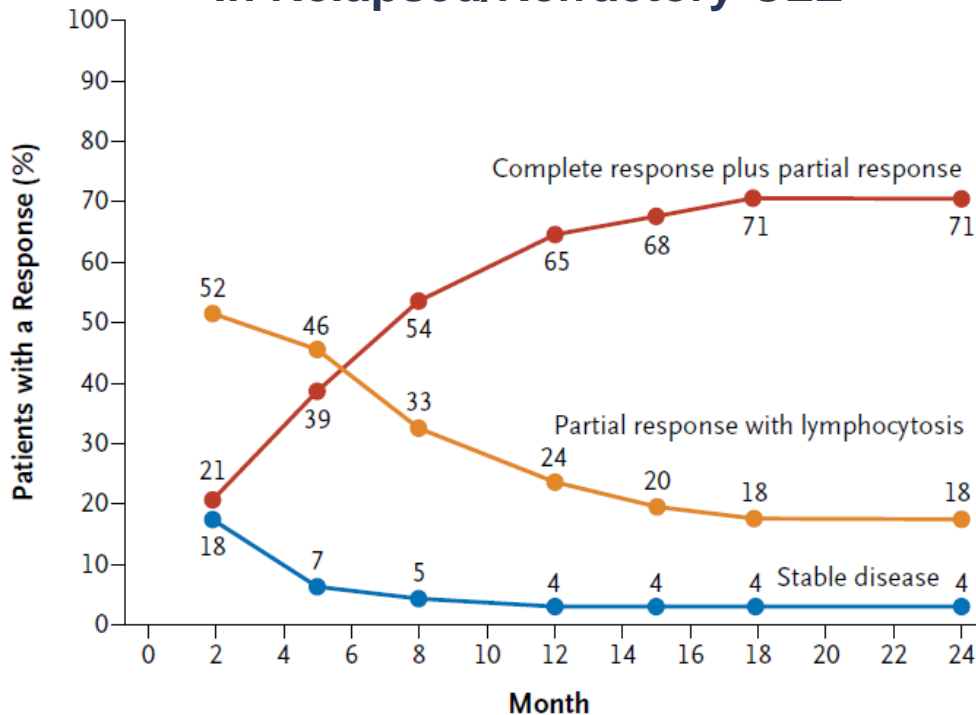


- Single arm study for patients with relapsed or refractory MCL and CLL per ibrutinib label
- Ibrutinib administered daily until off study, ublituximab administered through Cycle 6 only
- Study Chairs: Jeff Sharman, MD (CLL) and Owen A. O'Connor, MD, PhD (MCL)

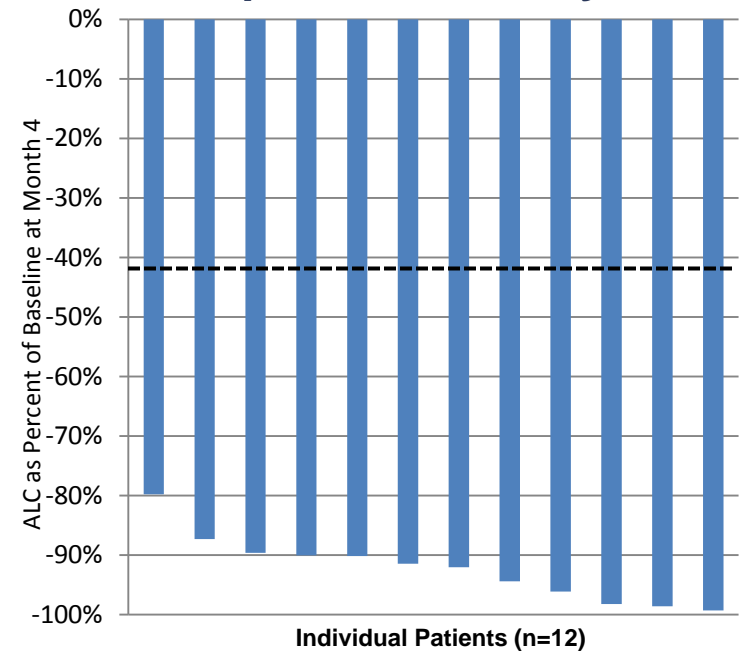
# Scientific Rationale: Ublituximab + Ibrutinib for CLL



## Ibrutinib Phase II In Relapsed/Refractory CLL



## Ublituximab Phase Ib In Relapsed/Refractory CLL

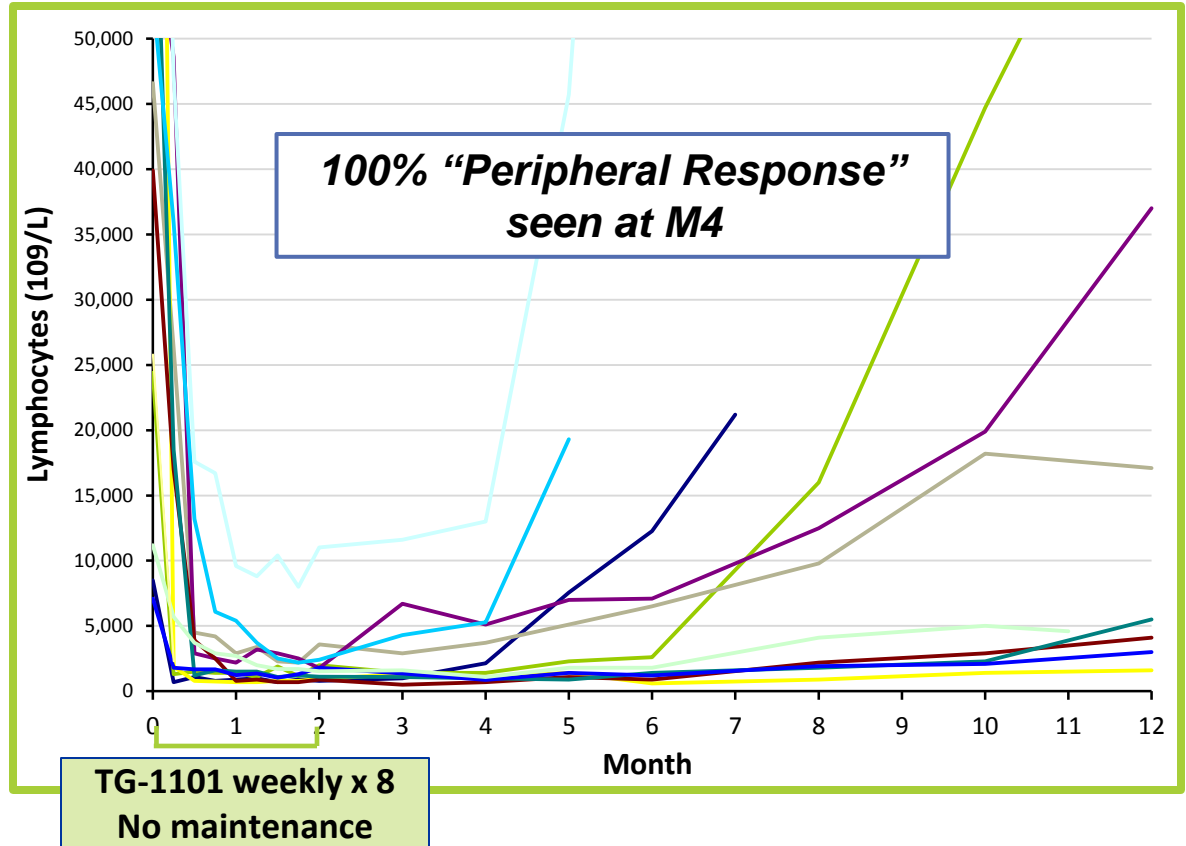


# TG-1101 in the Treatment of Rel/Ref CLL

## Phase 1b Efficacy Results



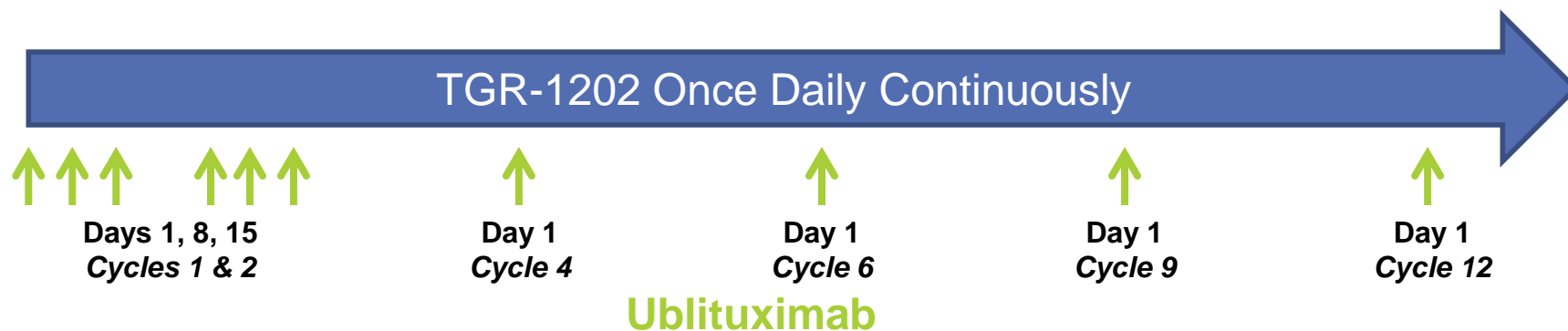
	Part II
Patients	12
Evaluable	11*
CR	0
PR at M4	7 (63.6%)
SD at M4	4
PD at M4	0
PR at M6	5 (45.5%)



- ▶ Overall response rate of **13%** (n=88) was observed in a rituximab single agent control arm in previously treated CLL/SLL patients.<sup>1</sup>

\*pt: premature withdrawal for secondary acute leukemia

# Phase I/II Study of TG-1101 + TGR-1202



- Single arm study, in patients with CLL and NHL relapsed or refractory to at least 1 prior regimen (no limit on prior therapies)
- Patients with prior experience with PI3K-delta and BTK inhibitors are NOT EXCLUDED
- Study Chairs: Susan O'Brien, MD (CLL) and Nathan Fowler, MD (NHL)

# TGR-1202

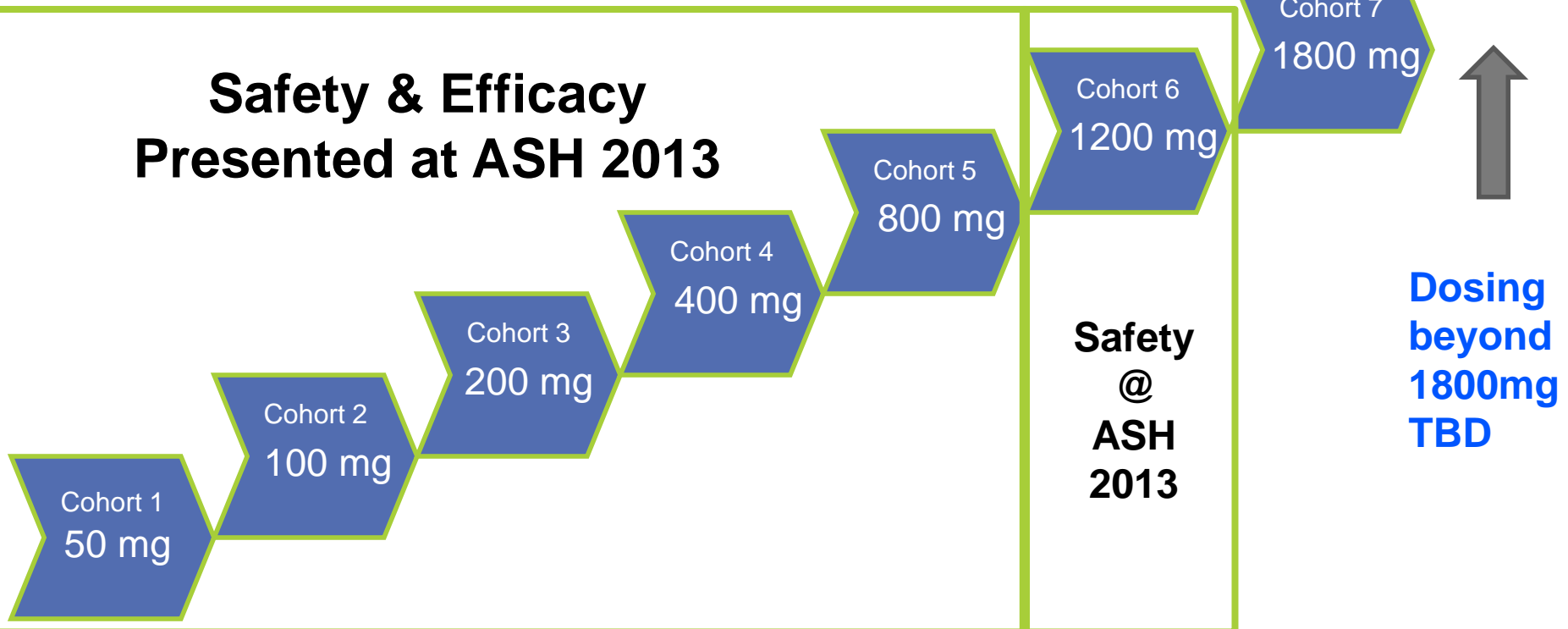
## (PI3K- $\delta$ INHIBITOR)

# Phase I First-in-Human Study of TGR-1202 Patients with Rel/Ref Hematologic Malignancies



- Includes Patients with Relapsed/Refractory Hematologic Malignancies
- No limit on prior therapies
- Continuous once daily oral dose (QD)
- Study Chair: Michael Savona, MD, Sarah Cannon Research Institute

## Safety & Efficacy Presented at ASH 2013

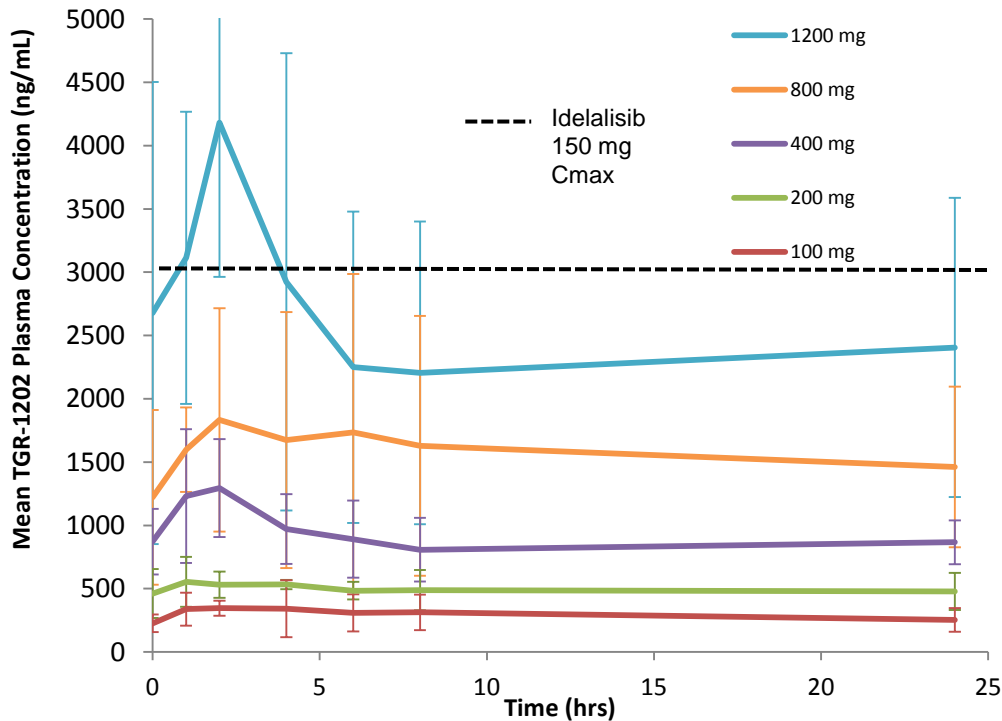


# TG 1202-101: ASH Poster Highlights

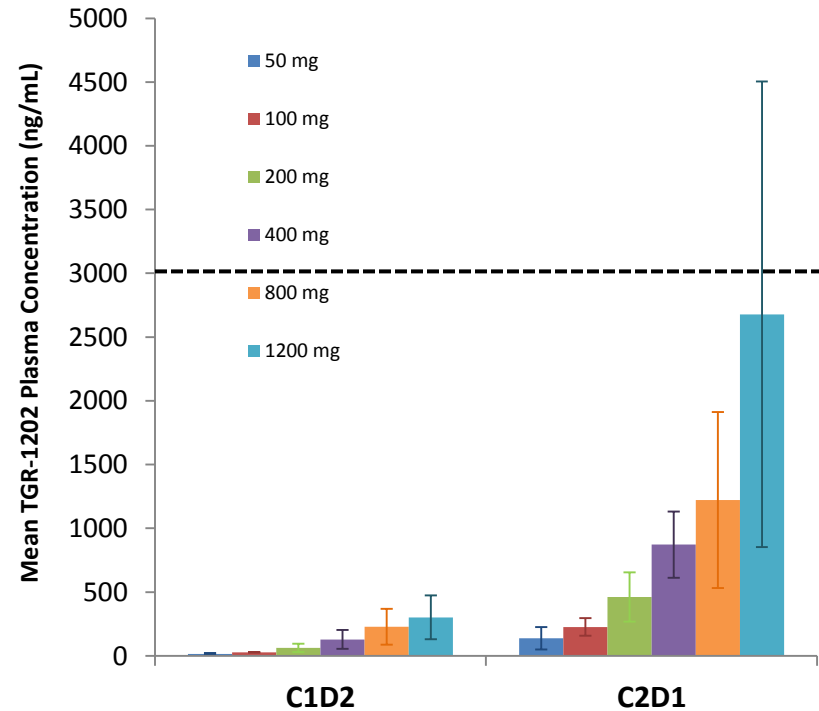


- **Poster Presented at ASH, December 2013**
- Well tolerated to date – no unexpected safety issues
- PK data so far continues to support once-daily dosing

Steady State (C2D1) 24-hr Plasma Concentrations



Pre-Dose Plasma Concentrations



## Definite, Probable, or Possibly Related AEs (N=22)

Adverse Event, n	Grade 1 & 2 (>5% of patients)	Grade ≥ 3 (all events)
Diarrhea	4	-
Neutropenia	-	1
Rash	-	1
Thrombocytopenia	-	1

- **One DLT observed at 800 mg QD:** Gr. 3 Rash deemed possibly related to TGR-1202.
  - Resolved upon temporarily holding study drug and concomitant medications
  - Did not reappear upon re-challenge at the same TGR-1202 dose level
- Of the 22 evaluable patients, one (CLL patient in Cohort 3 – 200 mg QD) was dose reduced due to an event of Gr. 3 neutropenia

## Gr. 3 & 4 Reported AEs – Any Causality (N=22)

Adverse Event, n	Grade 3	Grade 4
Dyspnea	1	-
Neutropenia	2	-
Rash	2	-
Thrombocytopenia	1	-
Lung Infection	1	-



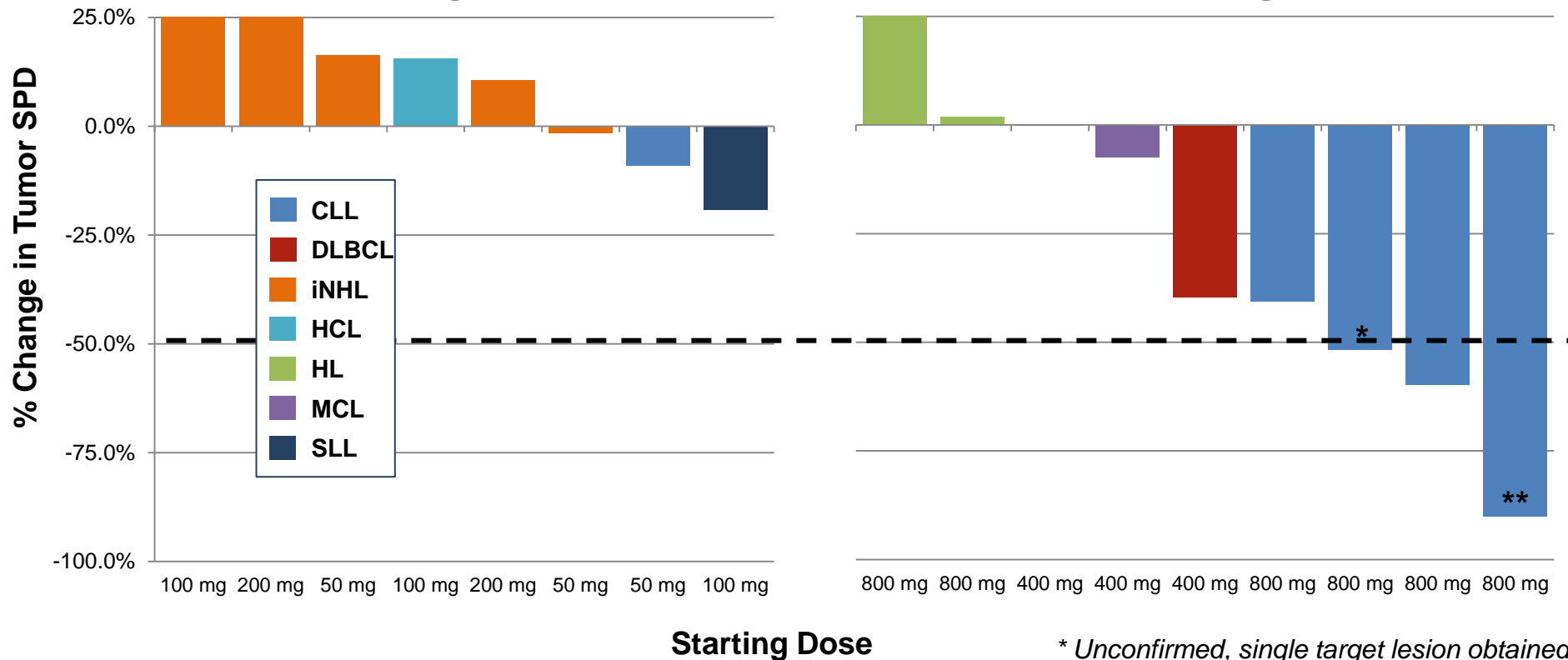
# TGR-1202: Efficacy



## % Change in Tumor Size At Week 8

< 400 mg QD

≥ 400 mg QD



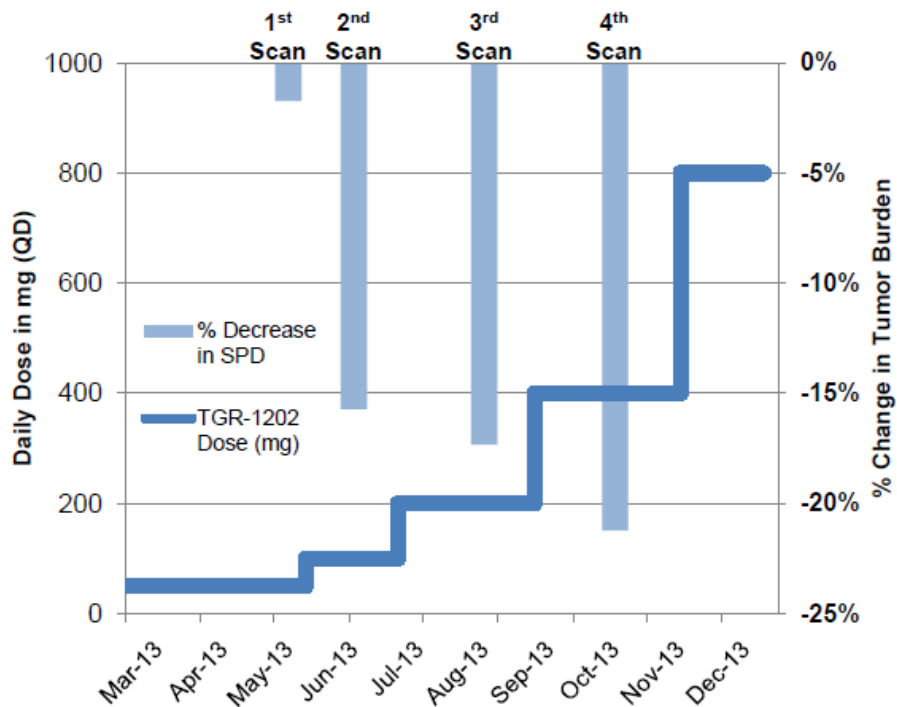
\* Unconfirmed, single target lesion obtained outside screening window  
 \*\* Assessment by Physical Exam only, not confirmed by CT

# TGR-1202: Dose/Time Dependent Responses

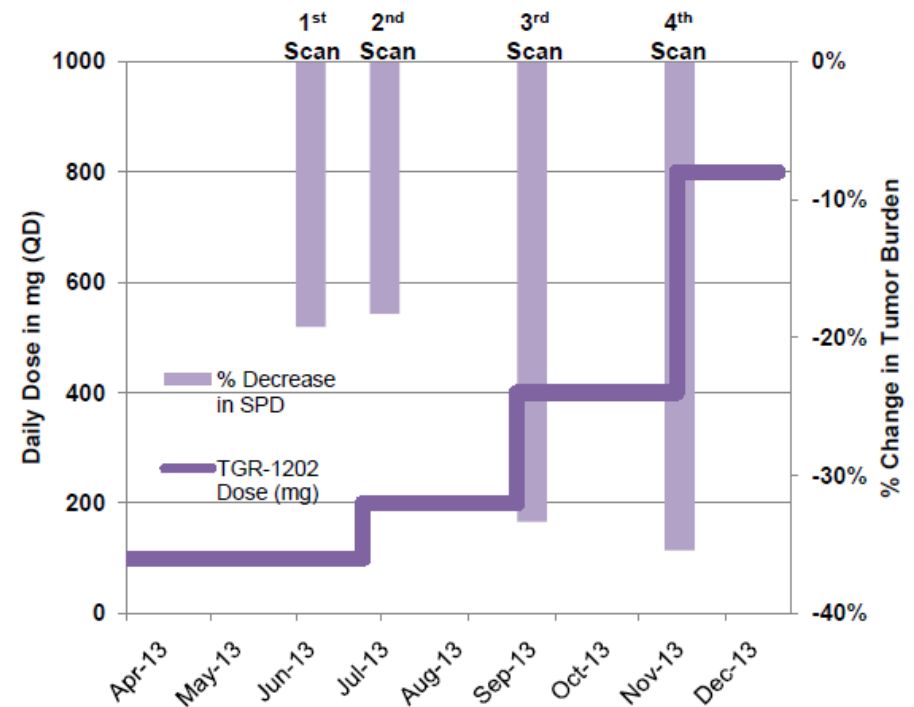


- Intra-patient dose escalation: all patients on study as of ASH 2013 currently being treated at 800 mg QD or higher.
- Early patients on study show decreasing tumor burden correlating with higher TGR-1202 dosing and extended duration of dosing:

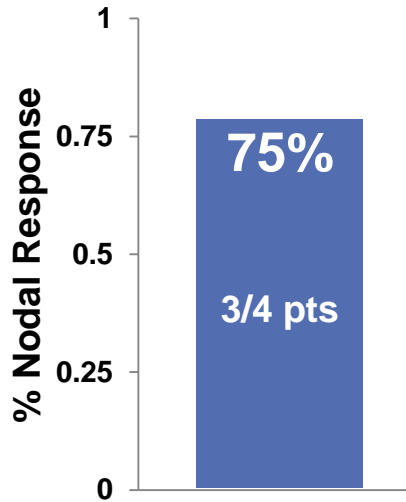
### Cohort 1 – FL Patient



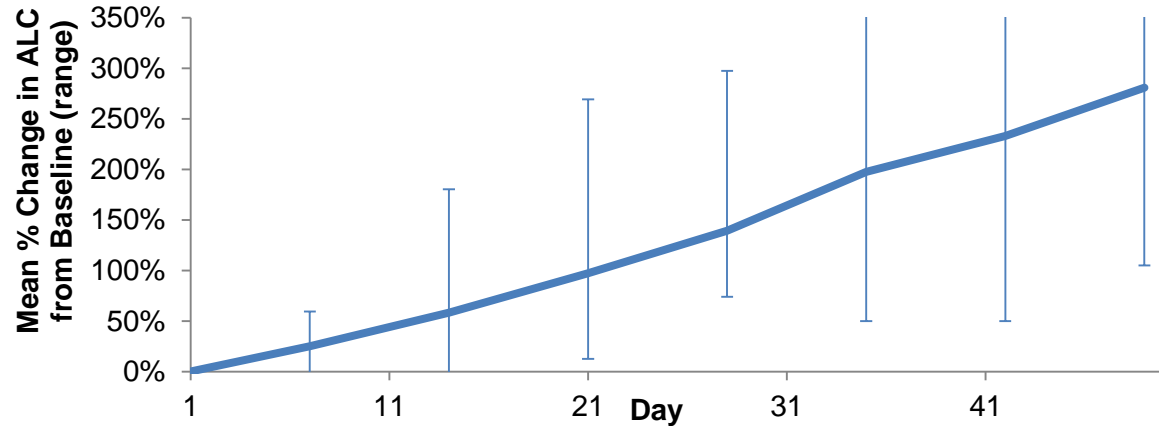
### Cohort 2 – SLL Patient



# TGR-1202: CLL Pts at 800 mg



**Nodal Responses and Marked Lymphocytosis in CLL patients treated with TGR-1202**



- 5 CLL patients enrolled at 800 mg (one off study within 1 Cycle due to Richter's transformation)
- Of the 4 remaining CLL patients, all had a nodal reduction
  - 3 nodal PR (> 50% LN reduction)
  - 1 nodal reduction of 41% by CT scan at Week 8

# TGR-1202: Preliminary Findings



- TGR-1202 is well tolerated with promising signs of clinical activity in the higher dosing cohorts
  - No dose-related trends in safety observed, and notably **no drug-related hepatotoxicity observed to date**
- TGR-1202 displays linear kinetics through 1200mg dose.
- **Steady-state half life >50 hours, supports once-daily (QD) oral administration of TGR-1202**
- Clinical activity observed at higher dose levels (>400 mg)
- No MTD has been achieved, and dose escalation continues at the 1800 mg QD dose level

# 2014 Milestones



<b>Q1 2014</b>	<b>Commence TG-1101 plus Ibrutinib combo trial in CLL</b>
<b>1H 2014</b>	<b>Determine optimal dosing for TGR-1202 as single agent</b>
<b>1H 2014</b>	<b>Enroll combo studies: 1101/1202 and Ibrutinib in CLL/MCL</b>
<b>Q2 2014</b>	<b>Present preliminary data from combo trials</b>
<b>Q2 2014</b>	<b>Presented updated single agent data for TG-1101 and TGR-1202</b>
<b>2H 2014</b>	<b>Commence combination registration trial(s)</b>
<b>Q4 2014</b>	<b>Present updated combo data</b>

## Key Statistics

**Ticker:**

**TGTX (NasdaqCM)**

**Price:**

**\$5.00**

**Shares:**

**~33M (Primary); ~39M (fully-diluted)**

**Cash:**

**~\$50M at September 30, 2013**

**Burn:**

**\$4-\$6M per quarter**

**Time:**

**24 months of cash**

- Greatly expanding market opportunity, driven by novel drugs and targets leading to dramatically better patient care and outcomes
  - \$10-\$15B market opportunity, with room and need for multiple treatment options
  - Serial lines of therapy and differentiated safety and efficacy profiles will create multiple winners
- Unequivocal activity of TG-1101 and TGR-1202, both with possibly best in class activity
- Multiple combination regulatory pathways for TG-1101 and TGR-1202
  - Enter pivotal trials in 2H14
  - Uniquely positioned to leverage multiple mechanisms



# TG Therapeutics

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