TG Therapeutics

NASDAQ: TGTX

May 2014

Forward Looking Safe Harbor Statement

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TG Therapeutics, Inc.

- Emerging biopharmaceutical company focused on cancer & autoimmune-related diseases

- Developing two drugs for B-cell cancers – CLL and NHL

  - **TG-1101** – Novel Glycoengineered, Anti-CD20 monoclonal antibody
    Same class as Rituxan®, which has ~$7BB WW Sales
    Enhanced ADCC profile for increased potency similar to Gazyva® (GA101)
    Single agent activity demonstrated in CLL and NHL in Phase 1/2 studies

  - **TGR-1202** – Novel PI3Kδ 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

Goal…non-chemotherapy-based combinations, with:

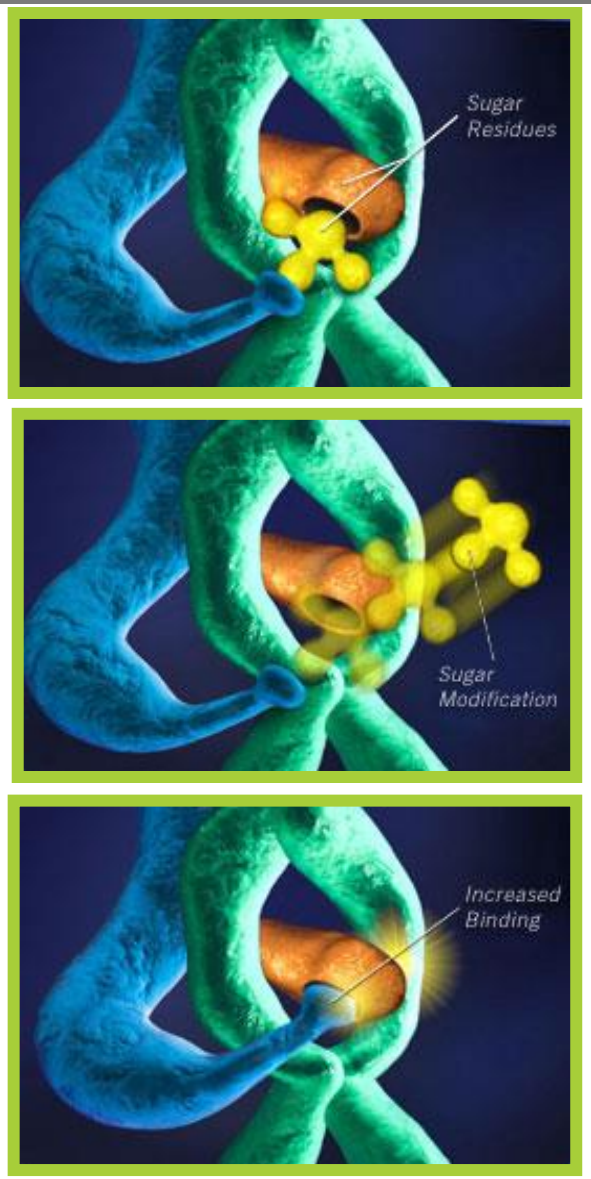
Glyco-engineered CD20s	BTK inhibitors	Delta inhibitors	Bcl-2 inhibitors
Gazyva	Ibrutinib	Idelalisib	Abt-199
TG-1101	CC-292	IPI-145	
	ONO-4059	TGR-1202	

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

TG-1101, a Novel Glycoengineered Anti-CD20

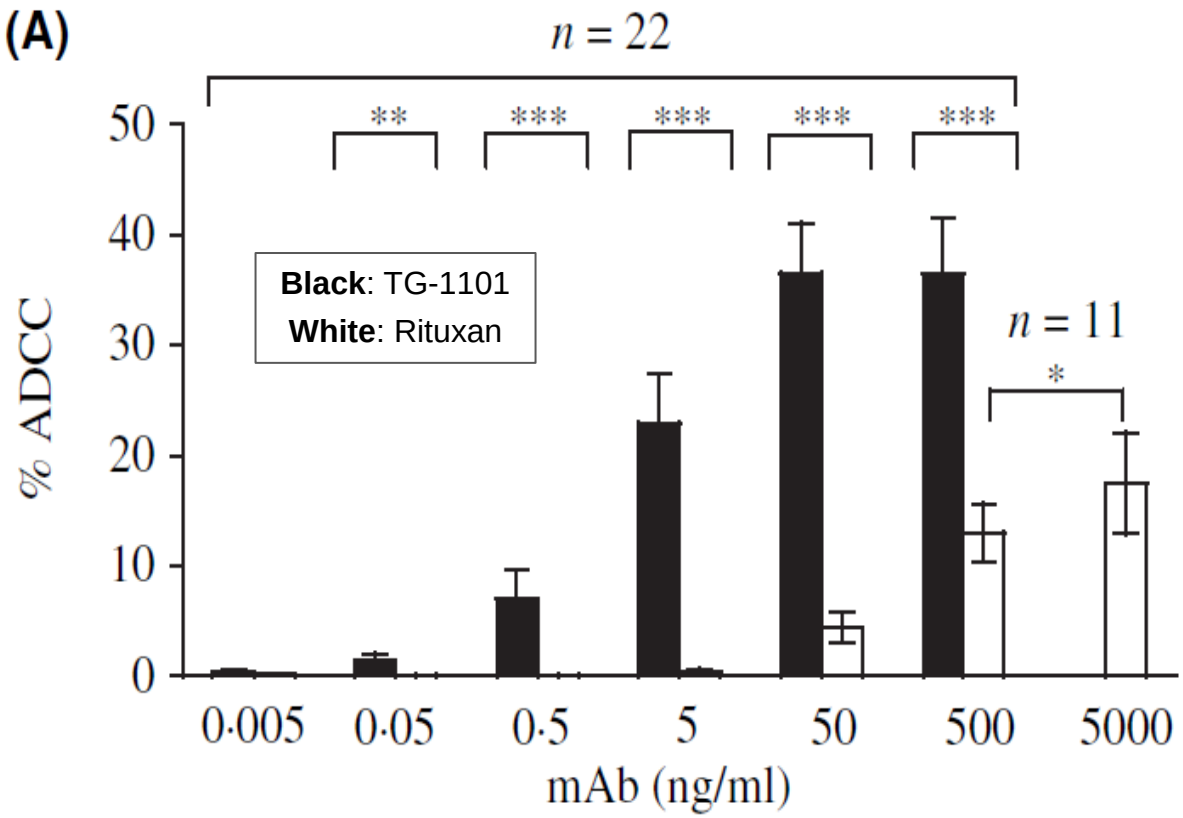
- TG-1101 Profile:
  - Novel protein sequence
  - Targets distinct epitope on CD20
  - Glycoengineered for enhanced activity
    - 50-100x the ADCC effects of RTX
    - comparable to GA101 in indirect comparisons
  - Demonstrated Single Agent activity in relapsed/refractory NHL & CLL

What is Glycoengineering?



Graphics courtesy of Genetech BioOncology

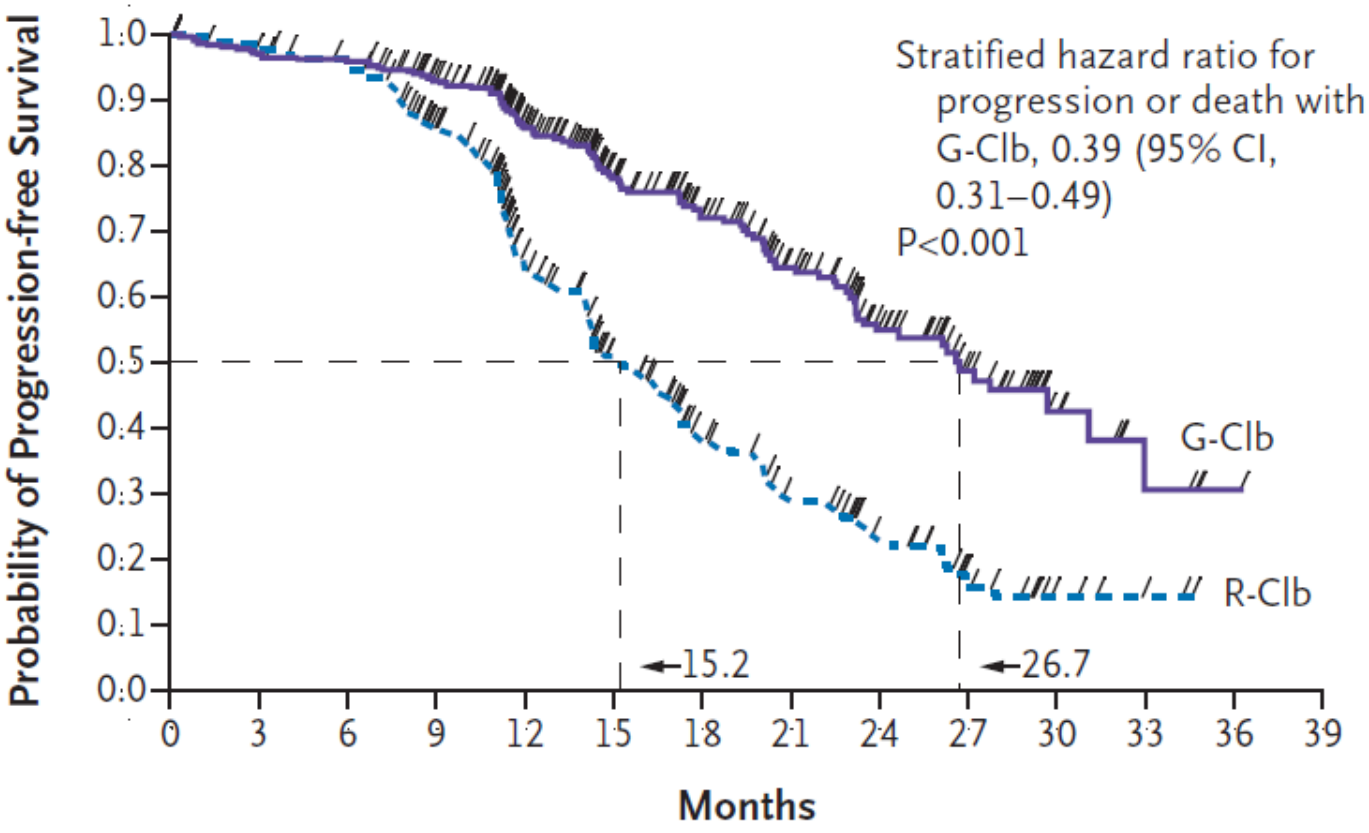
TG-1101 vs. Rituxan
ADCC Induction in CLL Patient Donor Cell Lines



Source: de Romeuf et al, 2008

Proof of Principle for Glycoengineering

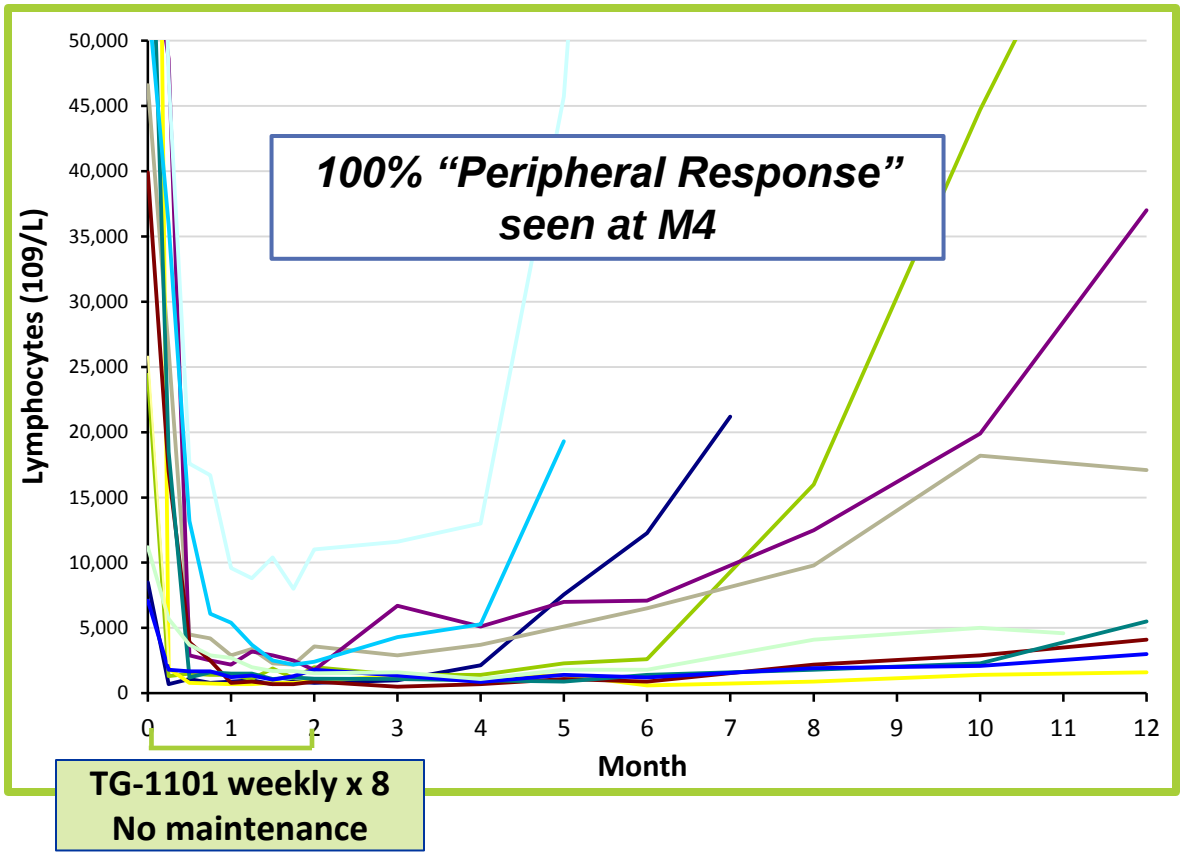
Ph III: GA101+Clb vs. RTX+Clb



Demonstrated single agent activity:

TG-1101 Phase 1b Efficacy Results Rel/Ref CLL

	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%)***



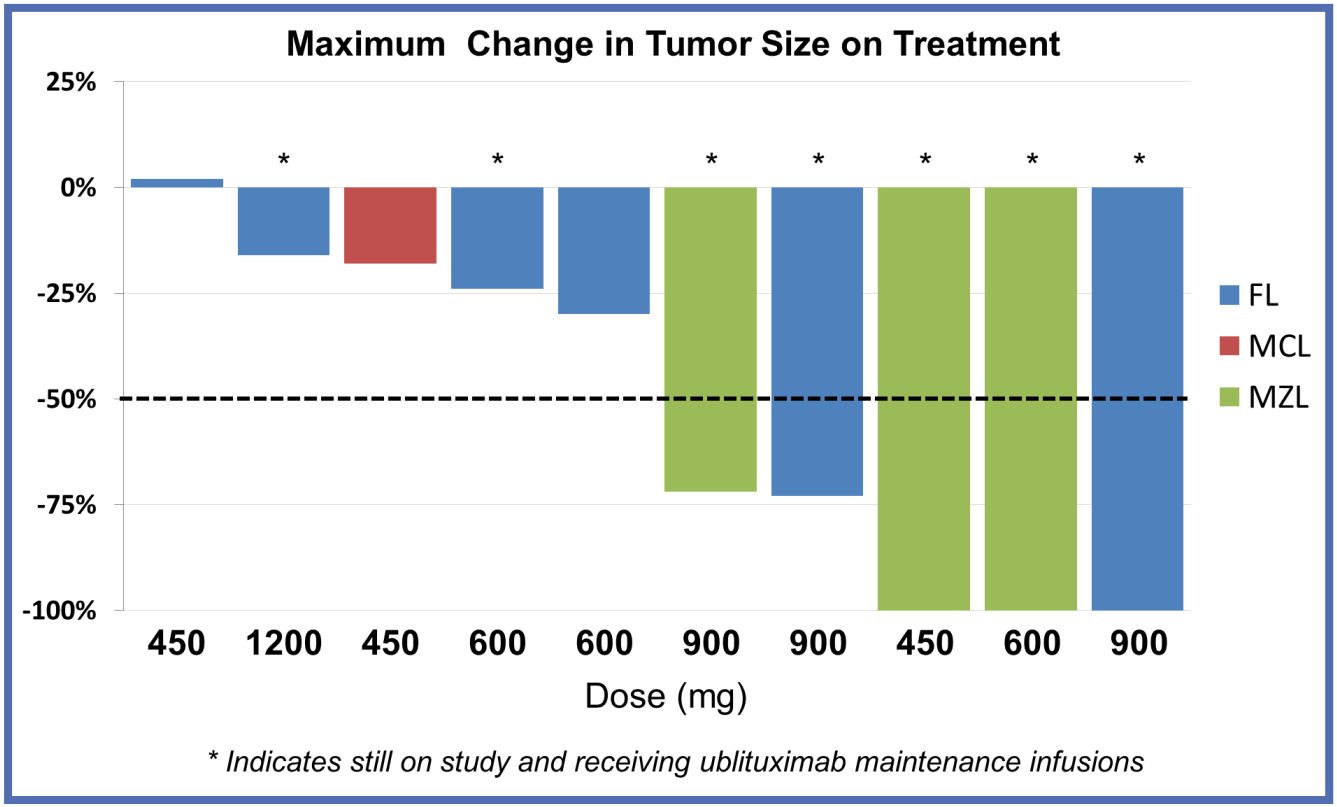
- Overall response rate of **13%** (n=88) was observed in a rituximab single agent control arm in previously treated CLL/SLL patients.[1]

*pt: premature withdrawal for secondary acute leukemia

[1]*Furman et al, ASH 2013*

Demonstrated single agent activity:
TG-1101 Phase 1 Efficacy Results in Rel/Ref NHL

- 10/12 patients were evaluable for efficacy (2 patients were too early for response assessment)
- 5 patients achieved an objective response (3 CRs, 2 PRs)
- ***Data to be updated at ASCO 2014***

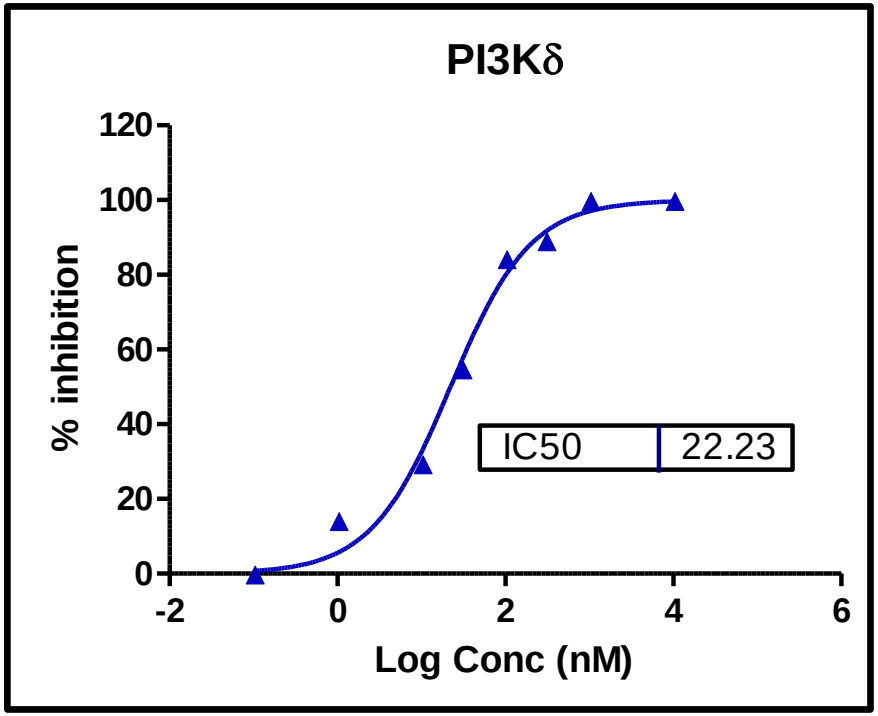


90% of evaluable patients had a reduction in target lesion

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
  - Once per day dosing
  - Prolonged half-life maintains target exposure over 24hour period
  - No drug related hepatotoxicity seen to date
  - Low incidence of GI toxicity and neutropenia, well-suited for multi-drug combinations

Enzyme Specificity

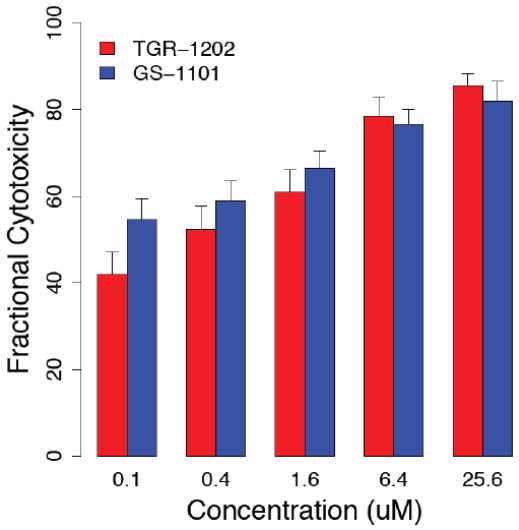


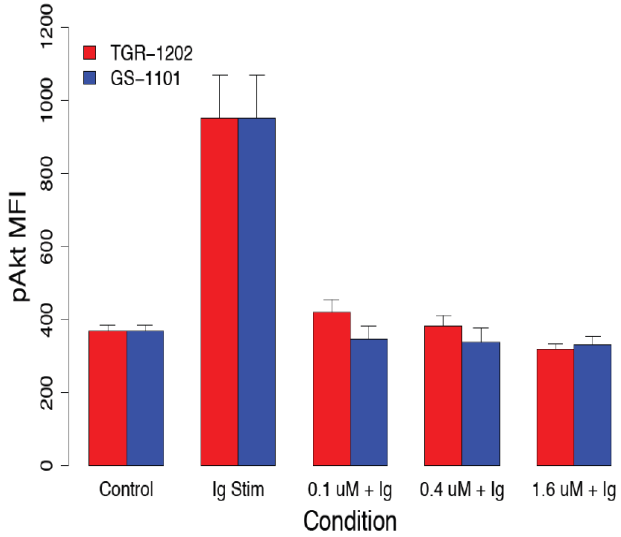
Fold-selectivity				
Isoform	α	β	γ	δ
TGR-1202	>10000	>50	>48	1
[1]Idelalisib	>300	>200	>40	1
[2]IPI-145	>640	>34	>11	1

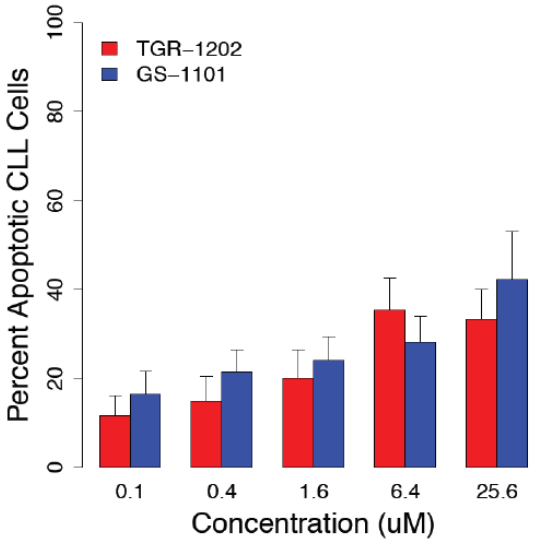
[1]Flinn et al. 2009, [2]Porter et al. 2012

TGR-1202 vs. Idelalisib

- Blinded *in vitro* study conducted at Duke University comparing TGR-1202 and Idelalisib in CLL patient cells (n=7)







Equivalent dose dependent cytotoxicity

Equivalent suppression of pAKT

Equivalent dose dependent induction of apoptosis

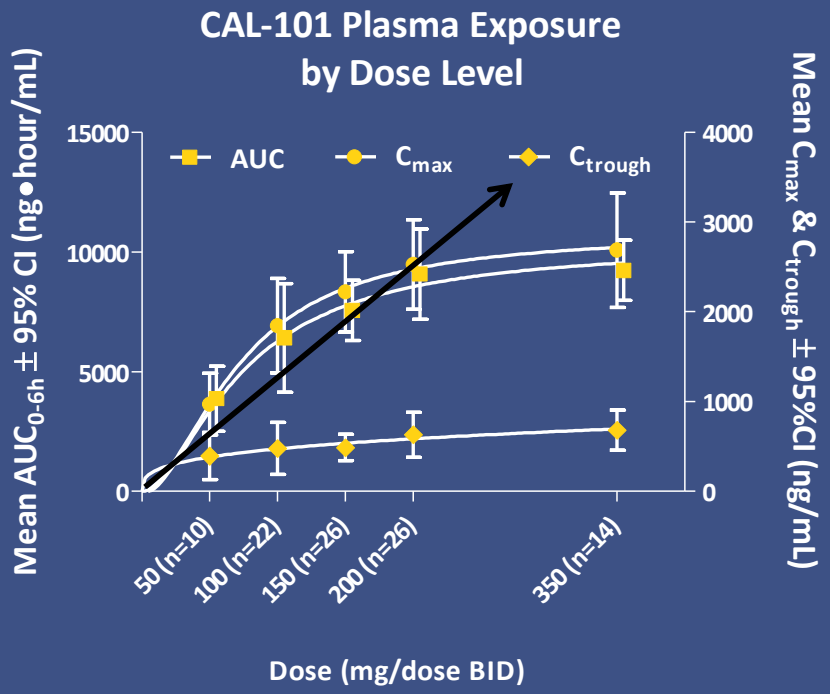
Friedman et al 2012, ASH Poster

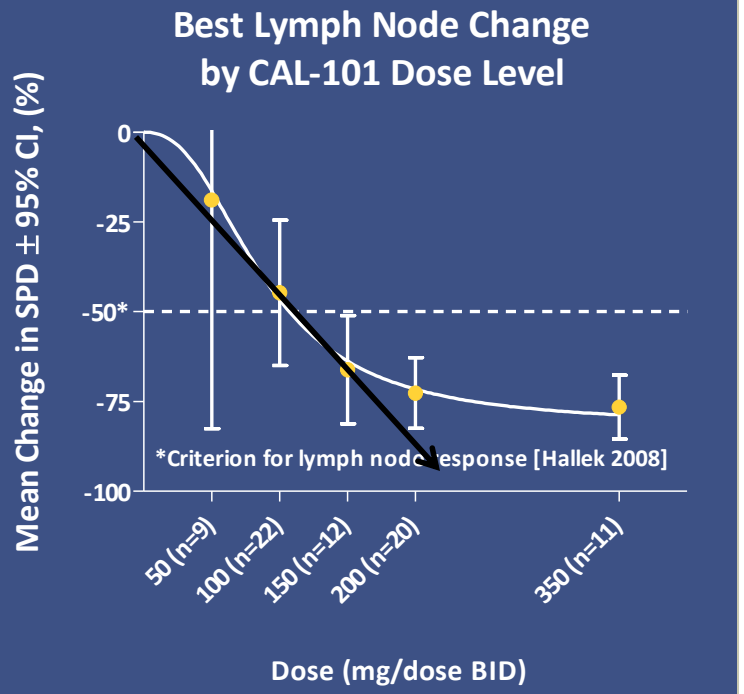
Room for Improvement

	Idelalisib	IPI-145
ORR - Rel/Ref CLL	**72% (CR=0%)**	**47% (CR=2%)**
CLL Toxicity Profile	fatigue, diarrhea, pyrexia, cough, back pain, rash AST/ALT elevation	neutropenia (majority Gr. 3 or 4), pyrexia, cough, rash, fatigue, diarrhea, AST/ALT elevation
ORR-Rel/Ref NHL	**58% (CR=0%)**	**68% (CR=16%)**
NHL Toxicity Profile	ALT/AST elevation (25% ≥Gr. 3), neutropenia (25% ≥Gr. 3) fatigue, diarrhea, nausea, rash	ALT/AST increase (majority Gr. 3), pyrexia, fatigue, cough, neutropenia (majority Gr. 3)

Horwitz et al; Patel et al; Benson et al, Brown et al ASCO 2013, Flinn et al, ASH 2013

Pharmacokinetic and Efficacy Data Illustrate Dosing Limitations with Idelalisib

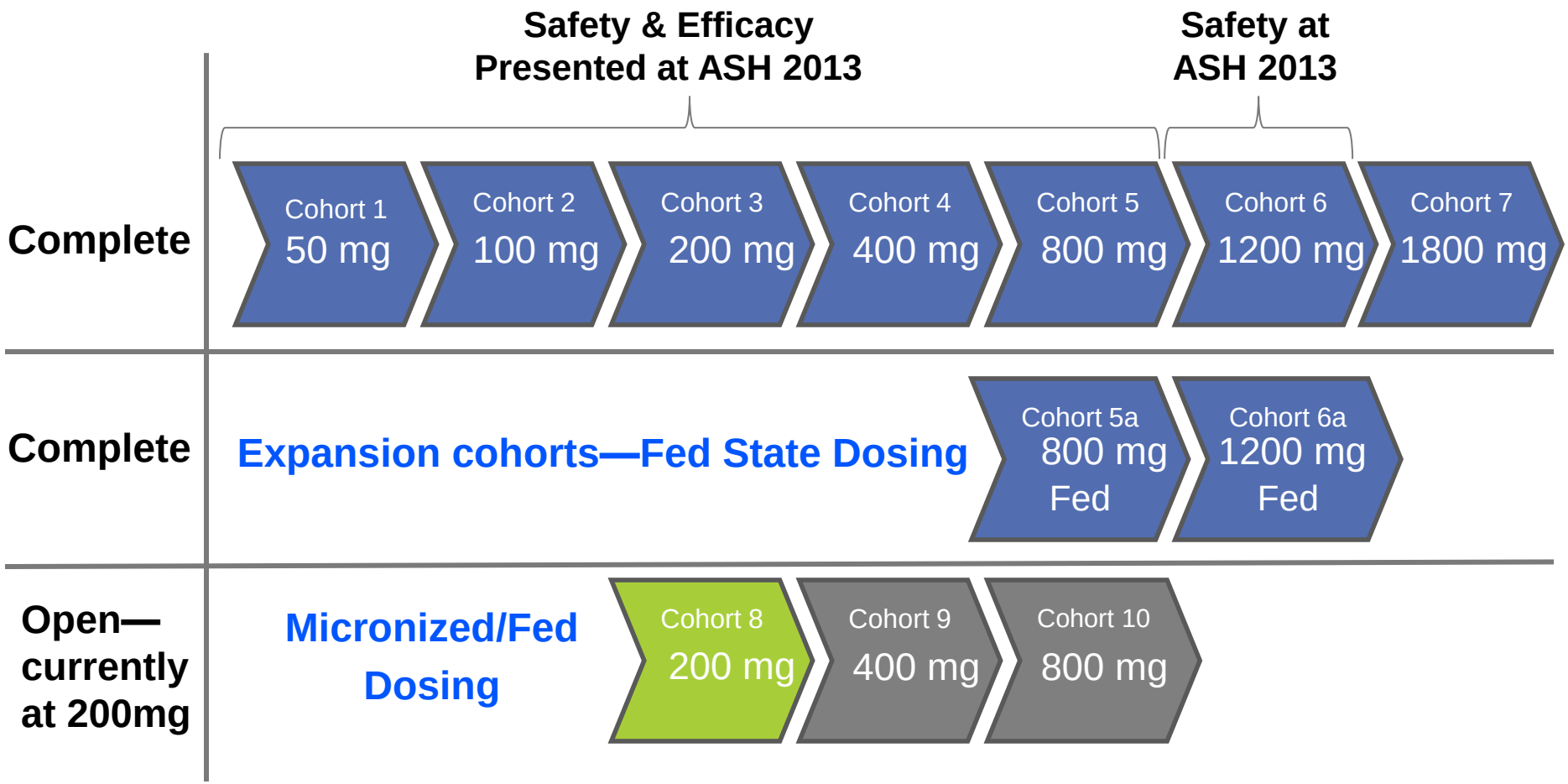




Dose-exposure relationships indicate little exposure gain at doses of >150 mg BID

Dose-response relationship suggests that at doses ≥150 mg BID, mean nodal shrinkage is >50% in most patients

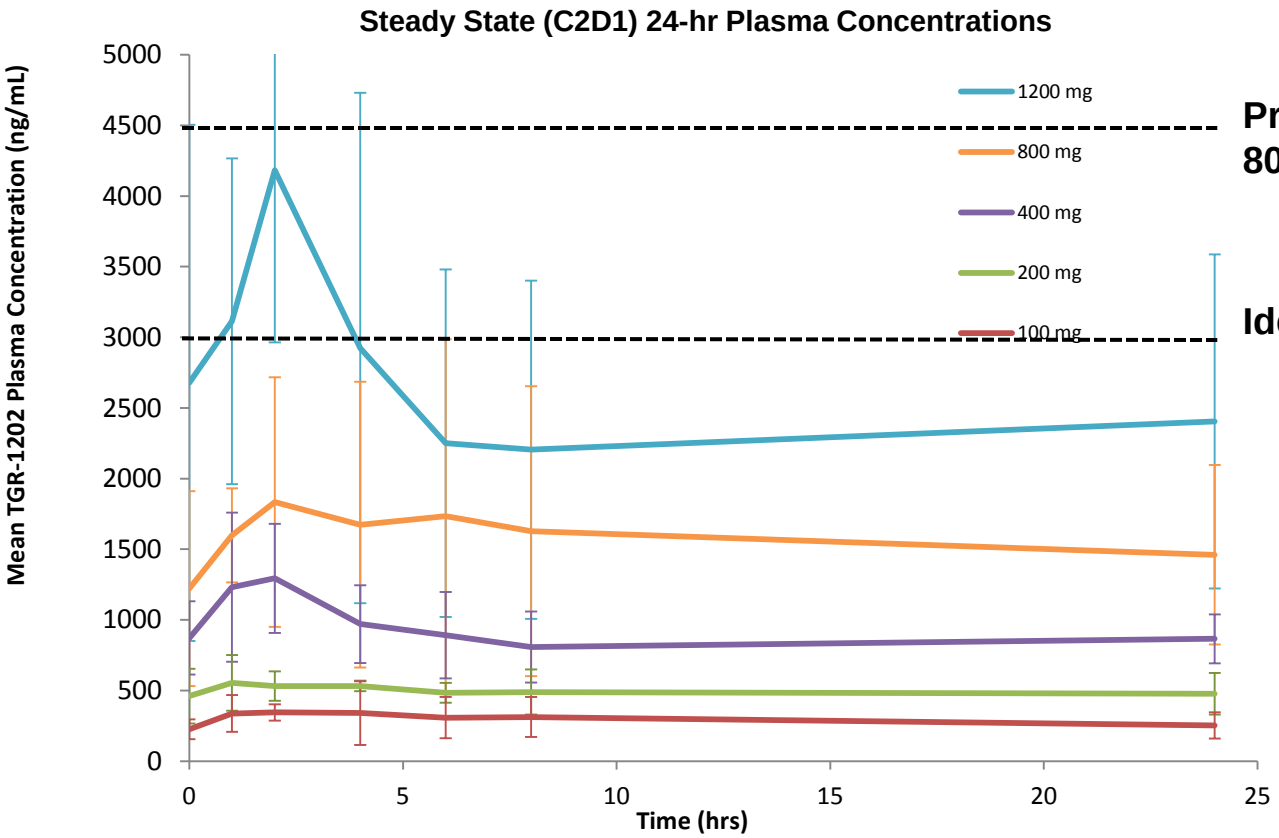
Phase I Study of TGR-1202
Enrollment and Progress Update



- ***<u>Micronized formulation & fed-state dosing projected to provide 3-4 fold increase in exposure levels</u>***

TG 1202-101: ASH Poster Highlights

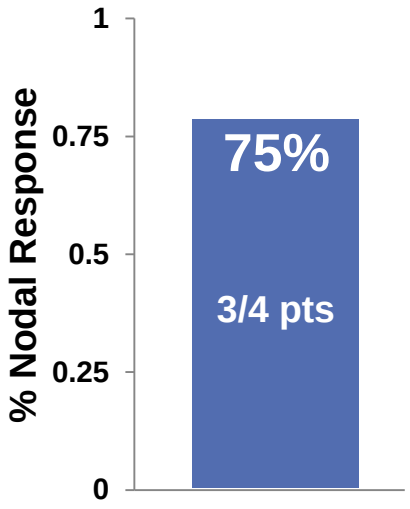
- **Poster Presented at ASH, December 2013**
- Well tolerated to date – no unexpected safety issues
- PK data supports once-daily dosing

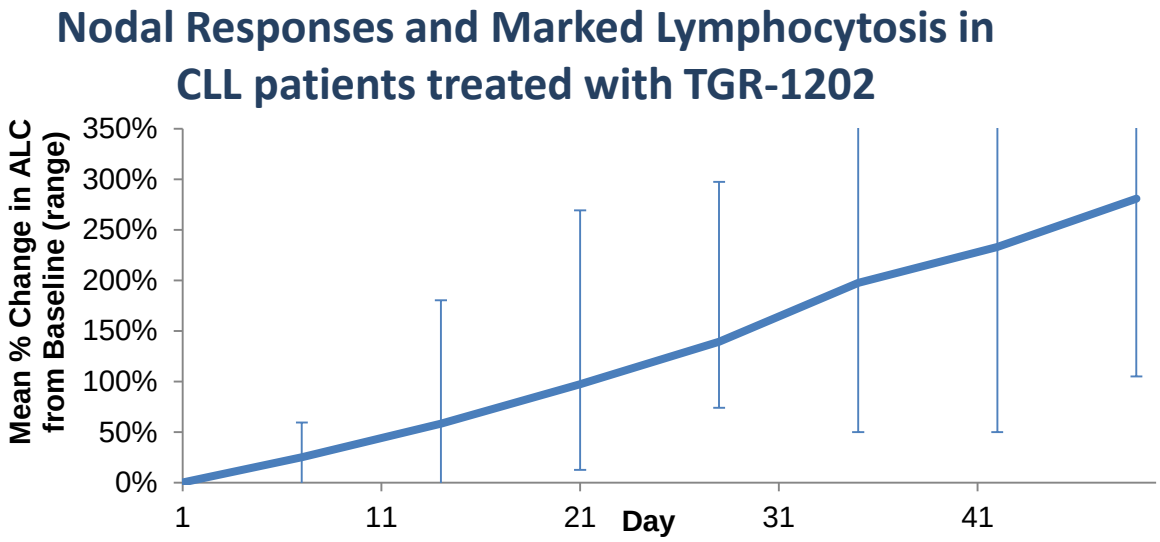


Projected trough levels for 600mg-800mg QD micronized fed

Idelalisib Cmax at 150mg BID

TGR-1202: CLL Pts at 800 mg





- 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

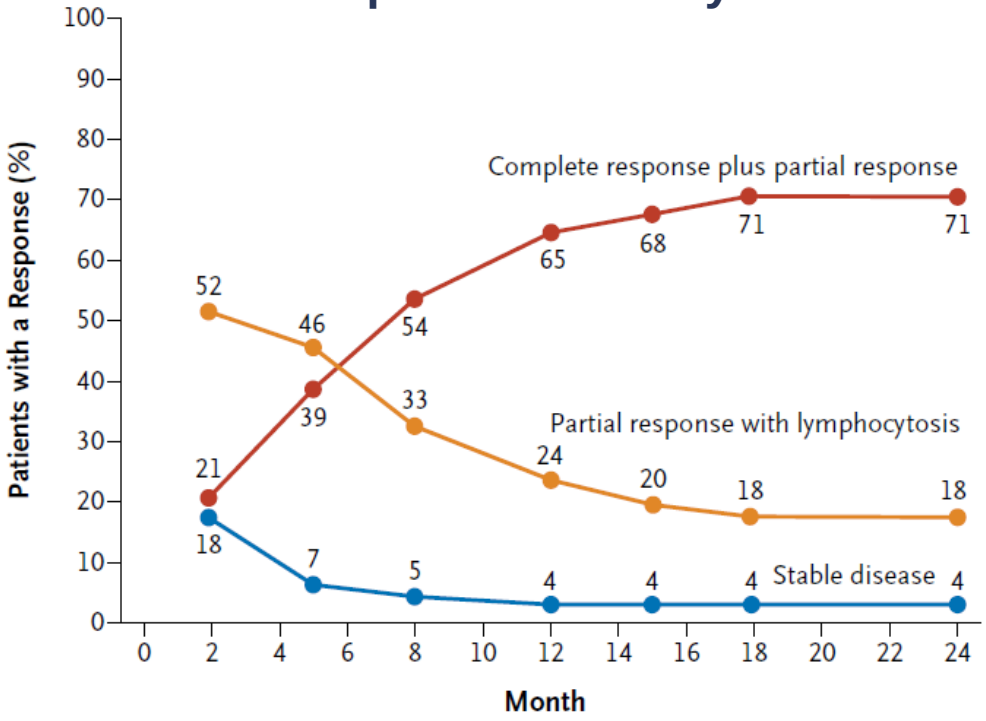
- TGR-1202 is well tolerated with promising signs of clinical activity in the higher dosing cohorts
  - No dose-related trends in safety observed, and notably **no drug-related hepatotoxicity observed to date**
- TGR-1202 displays linear kinetics through 1200mg dose.
- **Steady-state half life >50 hours, supports once-daily (QD) oral administration of TGR-1202**
- Clinical activity observed at higher dose levels (>400 mg)
- No MTD observed up through the 1800 mg QD dose
  - Micronized formulation & fed-state dosing change provides **increased exposure of ~3-4 fold over prior formulation/dosing** – restarting dose escalation at 200mg

Phase II Study of TG-1101 + Ibrutinib

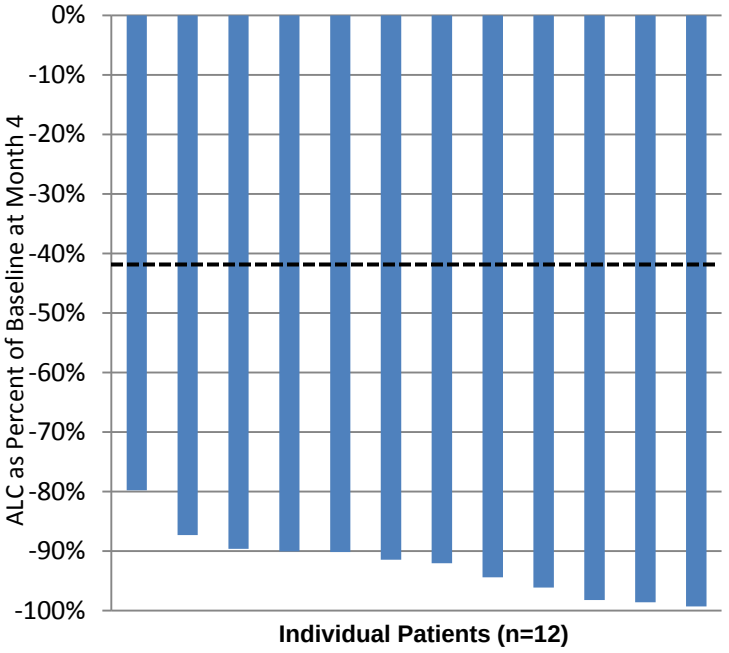
- Single arm study for patients with relapsed or refractory MCL and CLL per ibrutinib label
- Ibrutinib administered daily until off study, TG-1101 administered through Cycle 6 only
- Study Chairs: Jeff Sharman, MD (CLL) and Owen A. O'Connor, MD, PhD (MCL)

Scientific Rationale: TG-1101 + Ibrutinib for CLL

Ibrutinib Phase II In Relapsed/Refractory CLL



TG-1101 Phase Ib In Relapsed/Refractory CLL



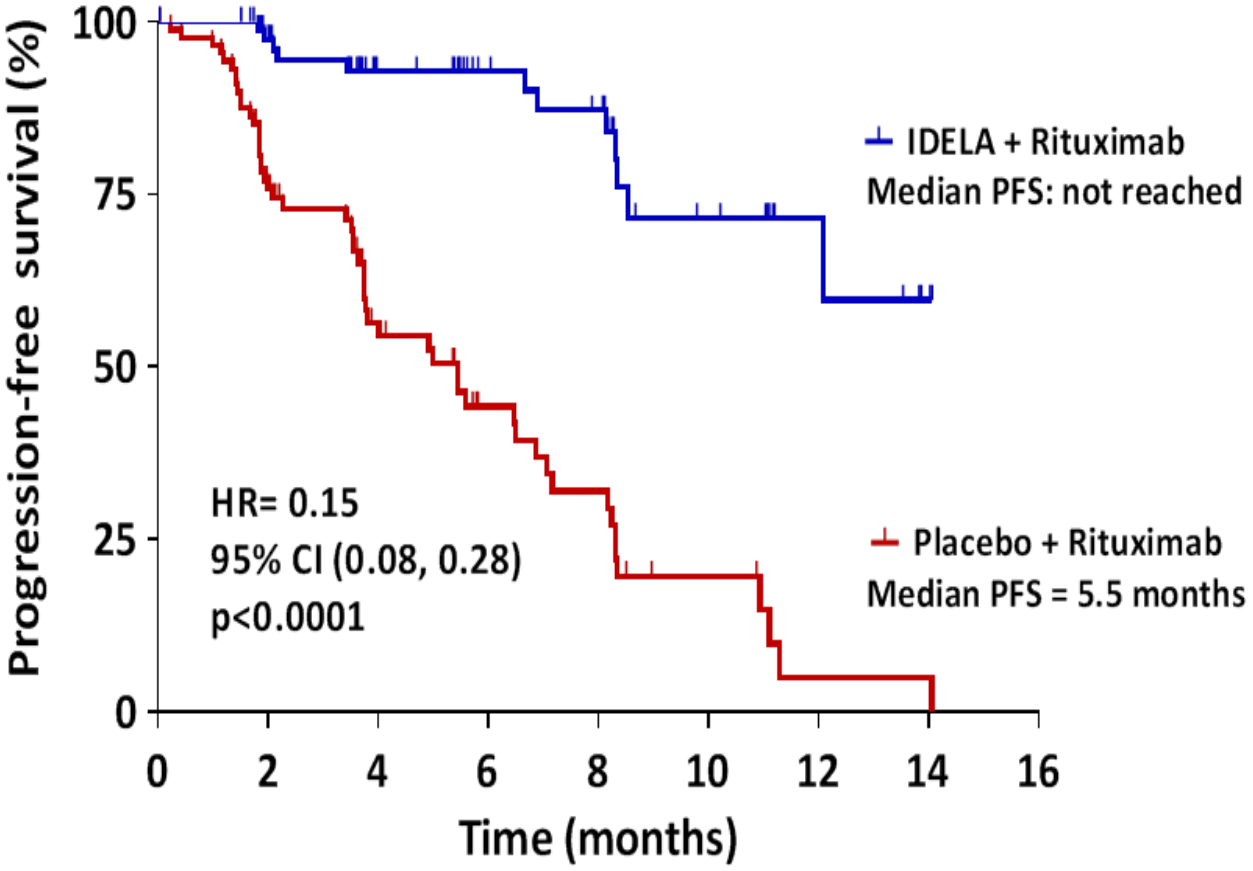
Byrd et al 2013 NEJM

Phase I/Ib 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)

Proof of Concept of Combination of CD20 plus PI3k-Delta inhibitor

Idelalisib + RTX vs. RTX



2014 Milestones

1H 2014	Determine optimal dosing for TGR-1202 as single agent
1H 2014	Enroll Ph. 2 TG-1101 + Ibrutinib in CLL and MCL
1H 2014	Enroll Ph. 2 TG-1101 + TGR-1202 in B-cell Malignancies
Q2 2014	ASCO - Present updated single agent data for TG-1101 & TGR1202
Q2 2014	EHA - Present prelim combo data for TG-1101 + Ibrutinib
Q3 2014	Pan-Pacific - Present prelim combo data for TG-1101 + TGR-1202
2H 2014	Commence combination registration trial(s)
Q4 2014	Present updated combo data and single agent TGR-1202 data

Corporate & Financial

Key Statistics	
Ticker:	**TGTX (NasdaqCM)**
Price:	**$5.50**
Shares:	**~37M (Primary); ~43M (fully-diluted)**
Cash:	**~$45.4M at December 31, 2013; plus $16.8M net offering proceeds**
Burn:	**$4-$6M per quarter**
Time:	**24+ months of cash**

Key Takeaways

- Greatly expanding market opportunity, driven by novel targeted drugs with dramatically better 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 attributes
- 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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