TG

TG Therapeutics

NASDAQ: TGTX

33rd Annual JP Morgan Healthcare Conference

January 2015

Forward Looking Safe Harbor Statement

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TG Therapeutics, Inc.

Leaders in developing drugs for B-cell cancers – CLL and NHL – as well as B-cell disorders (e.g. RA, MS, Lupus)

Pipeline designed for multiple combinations for best outcomes:

TG-1101 – Novel glycoengineered, anti-CD20 monoclonal antibody

- *Phase 3 in combination with ibrutinib pursuant to SPA*

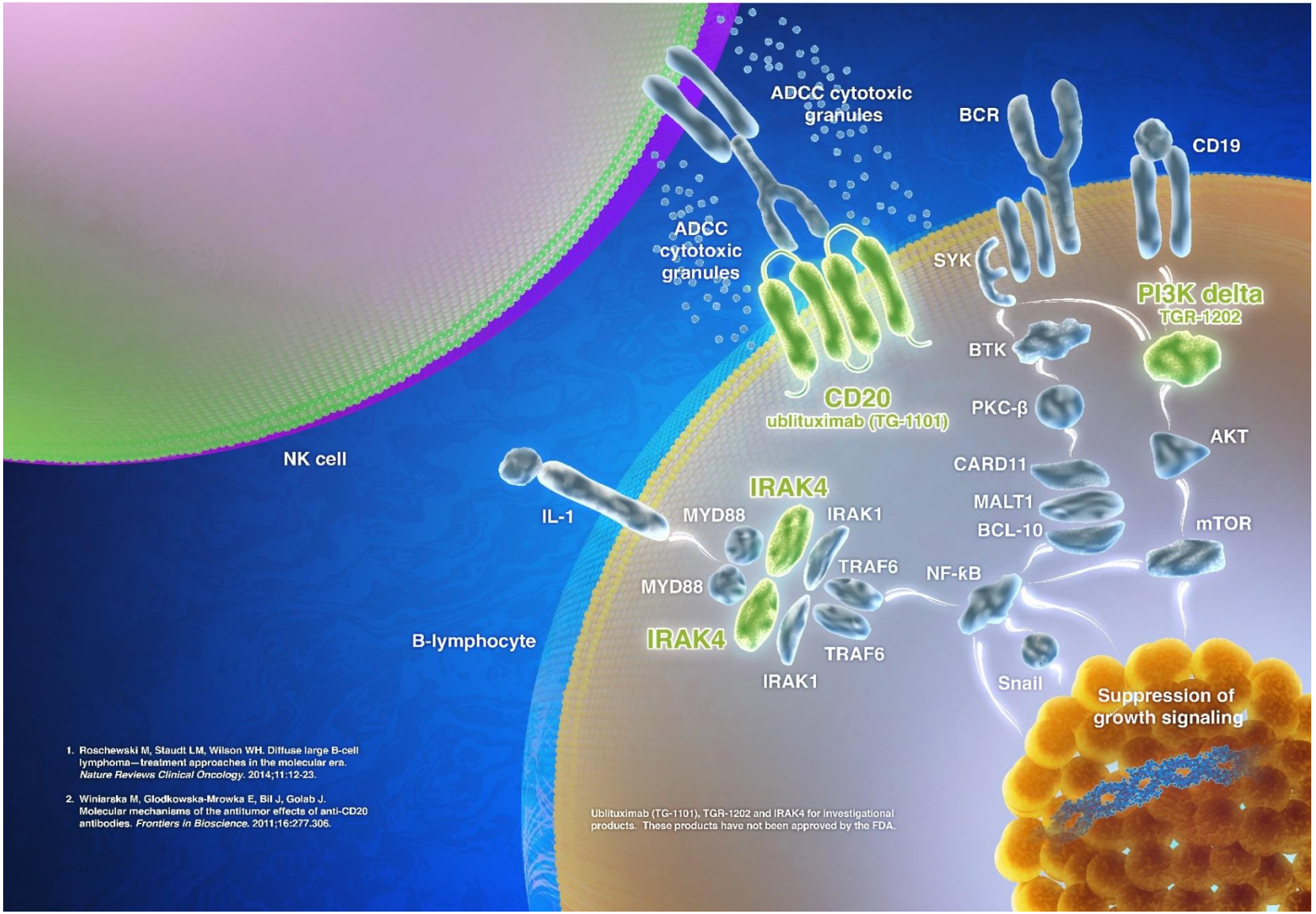
TGR-1202 – Once-daily PI3Kδ inhibitor

- *The only once-daily PI3Kδ inhibitor devoid of observed liver toxicity to date*

IRAK4 – Key signaling pathway independent of B-cell receptor

- *Potential for synergistic combinations with other pipeline products*

The Malignant B-cell is the Enemy…
Attacking multiple targets for better outcomes



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
    - Roche has previously reported superiority of GA101 based regimen vs. Rituxan in CLL
  - Demonstrated Single Agent activity in relapsed/refractory NHL & CLL with favorable safety profile
    - ~50% ORR in patients with CLL

TGR-1202, a novel Pl3k-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 24-hour period
  - ***No single-agent drug related hepatotoxicity seen to date;*** low incidence of GI toxicity and neutropenia, well-suited for multi-drug combinations
  - Highly active with ~90% of CLL patients achieving nodal PR and ~50% ORR in CLL patients

TG-1101 + ibrutinib - Safety

All Causality AE's in > 5% of Patients (n=54)		
Adverse Event	**All Grades** n (%)	**Grade 3/4** n (%)
Infusion reaction	18 (33%)	3 (6%)
Diarrhea	15 (28%)	2 (4%)
Fatigue	14 (26%)	1 (2%)
Rash	11 (20%)	2 (4%)
Bruising	8 (15%)	-
Nausea	8 (15%)	-
Mucositis	8 (15%)	-
Cough	7 (13%)	-
Edema	7 (13%)	-
Fever	6 (11%)	-
Thrombocytopenia	6 (11%)	2 (4%)
Neutropenia	3 (6%)	3 (6%)

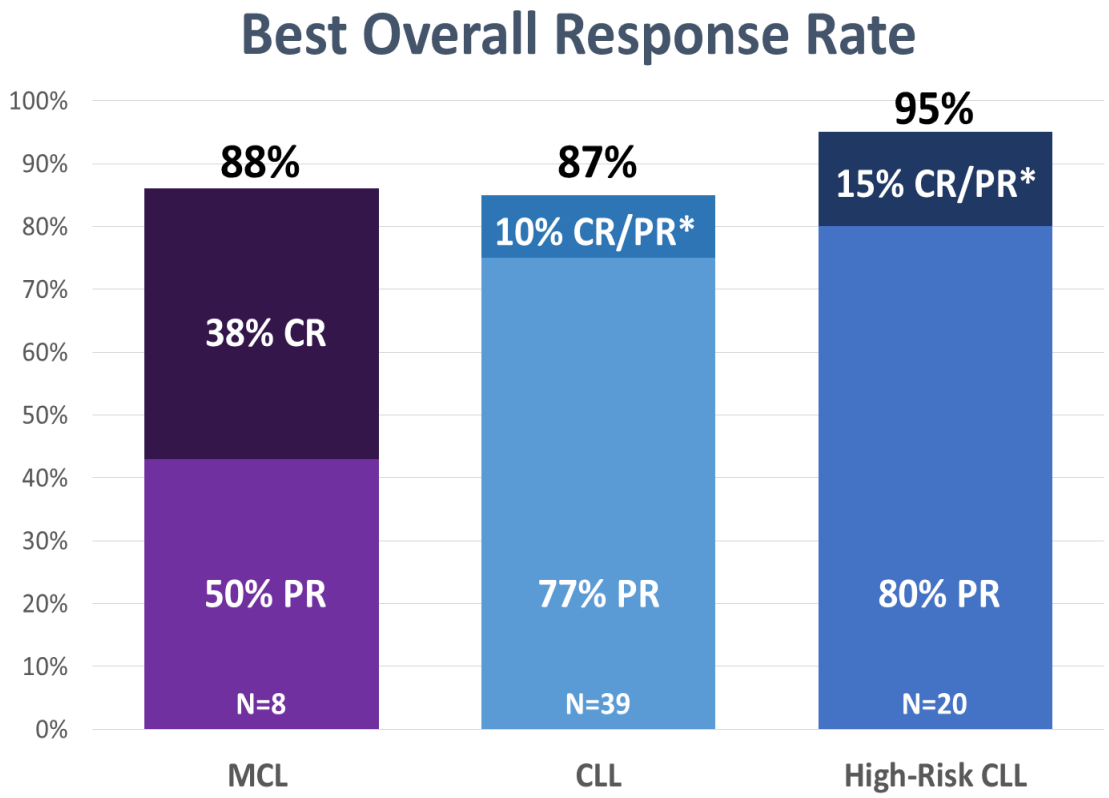
- All rash and Grade 3/4 diarrhea events deemed related to ibrutinib per investigator assessment.

Dose Reductions & Treatment Discontinuations

- Ibrutinib dose reduced in 4 patients (diarrhea, rash, cough, fatigue)
- No patients had their ublituximab dose reduced
- 2 patients discontinued due to ibrutinib related AEs (rash, diarrhea)
- 2 patients discontinued due to non-related AEs (pre-existing AE's)

Sharman et al, ASH 2014

TG-1101 + ibrutinib - Efficacy



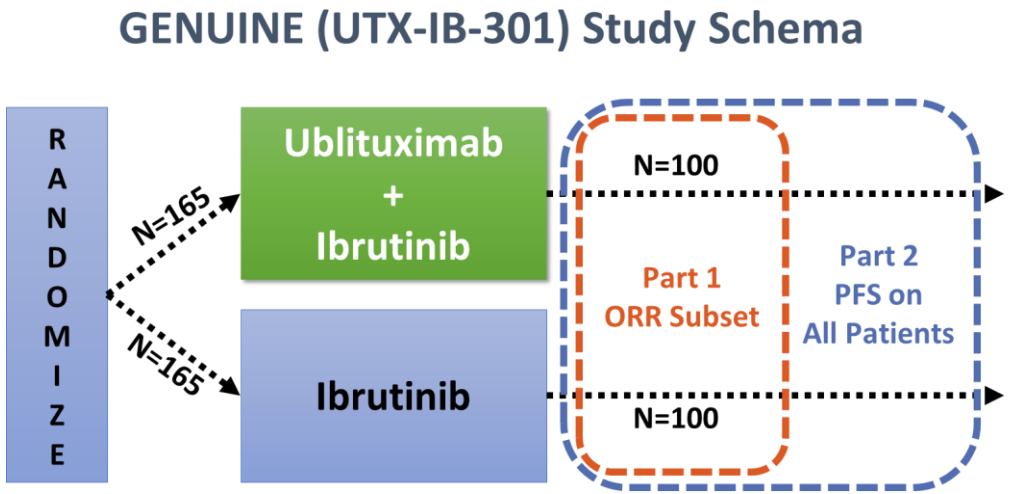
From ibrutinib label:

The ORR was **58.3%** (95% CI: 43.2%, 72.4%), all partial responses. ***None of the patients achieved a complete response***

- 30% of patients were considered anti-CD20-refractory, progressing on or within 6 months of an anti-CD20 based regimen
- Prior anti-CD20 therapy included rituximab, ofatumumab, and obinutuzumab
- In contrast to *in-vitro* reports, it does not appear that ibrutinib antagonized the ADCC effects of TG-1101

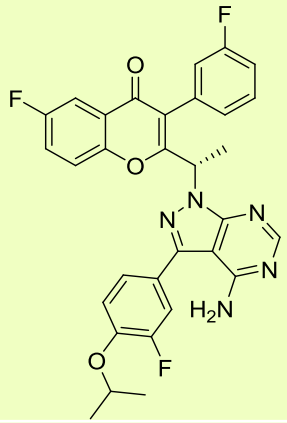
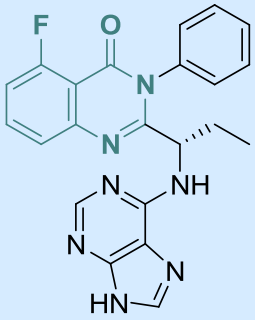
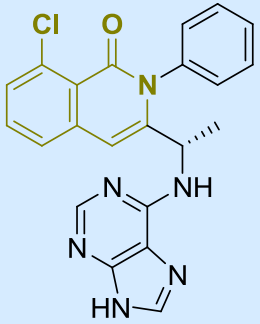
TG-1101 + ibrutinib - Phase III Clinical Trial

GENUINE
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB PLUS IBRUTINIB
Phase 3 Clinical Trial



- Design, Endpoints, and Statistics agreed to via Special Protocol Assessment (SPA)
- Enrolling ~330 patients with high-risk CLL, *anticipated 18-24 months to complete*
- ORR amongst first 200 patients for accelerated approval
- PFS amongst all enrolled patients for full approval
- Study Chair: Dr. Jeff Sharman

TGR-1202: Novel PI3Kδ (delta) Inhibitor

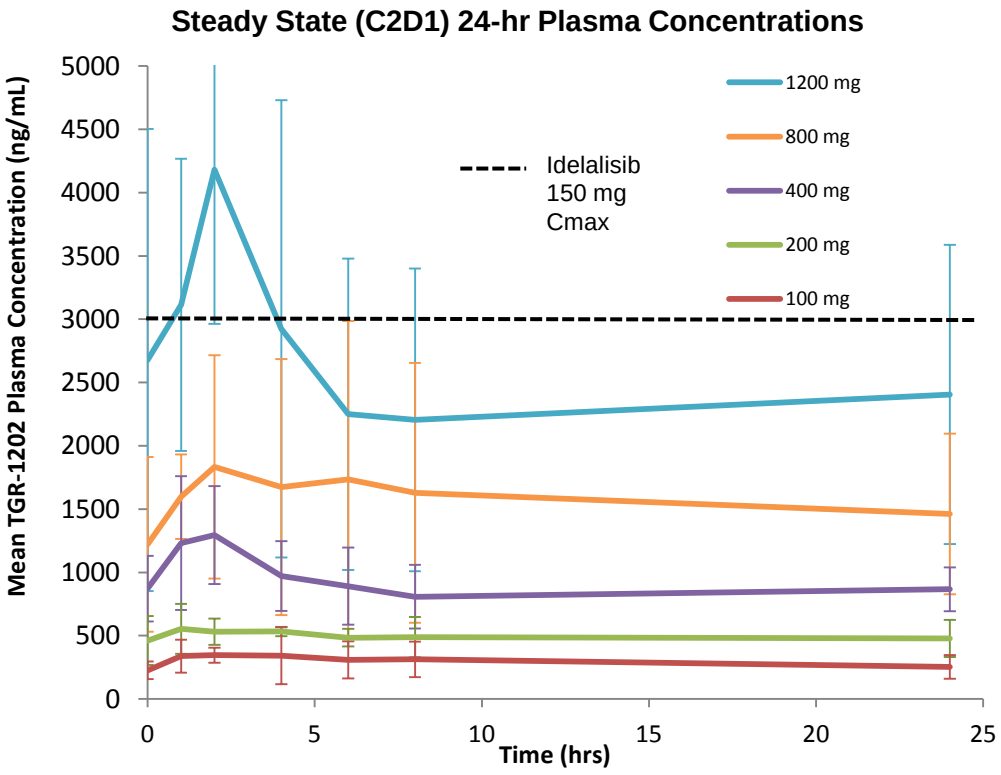
TGR-1202	Idelalisib (GS-1101)	Duvelisib (IPI-145)
		
QD	BID	BID

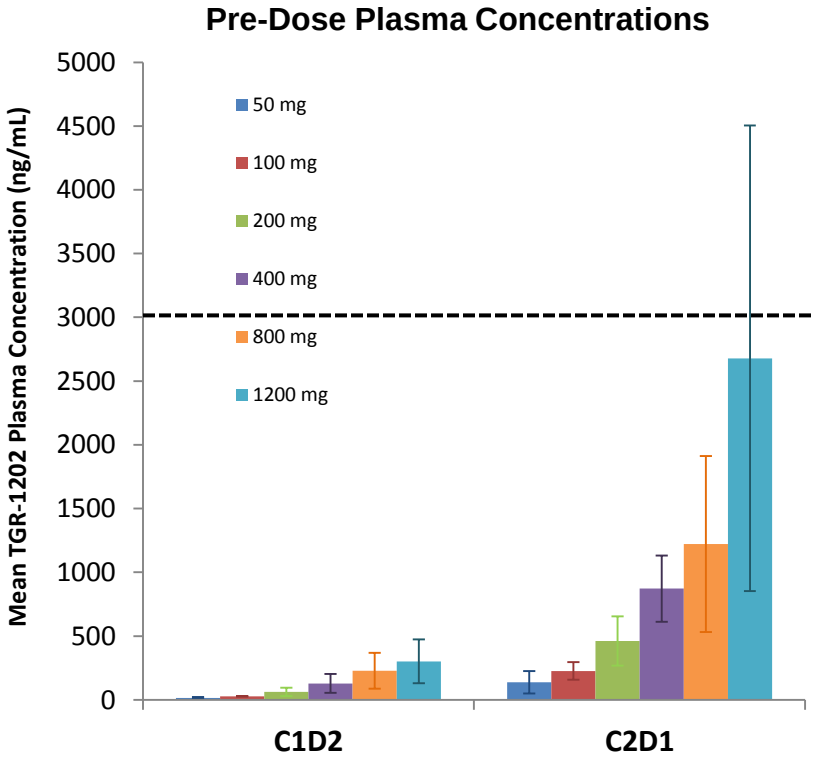
- PK profile that allows once-daily oral dosing
- Absence of hepatic toxicity in rel/ref hematologic malignances[1]
- 93% nodal PR rate in patients with rel/ref CLL[1]
- Dose escalation ongoing—dose-response relationship observed[1]

[1]Burris et al, ASH 2014, Abstract # 1984

TGR-1202 - PK *(as presented JPM '14)*

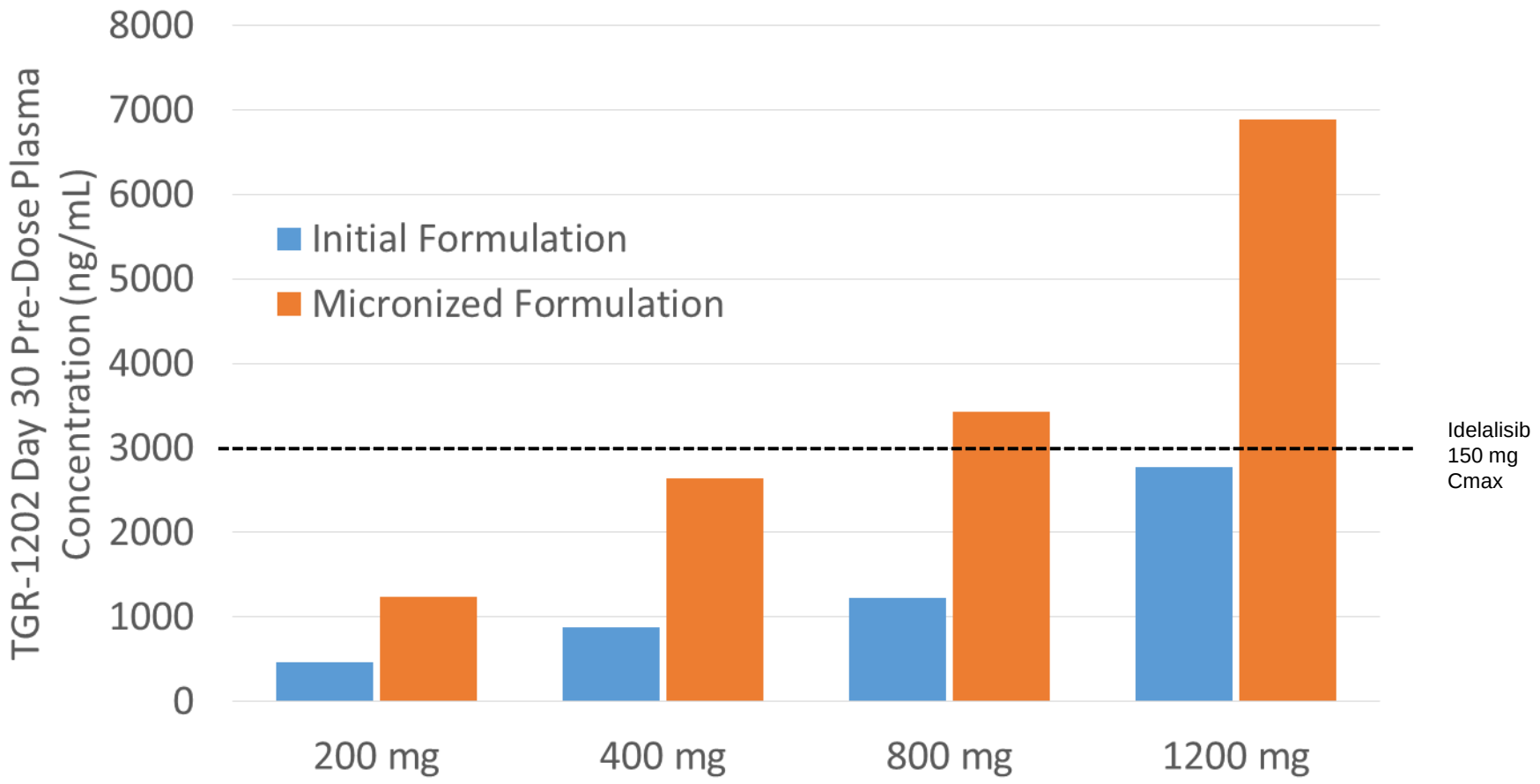
- **Poster Presented at ASH, December 2013**
- Well tolerated to date – no unexpected safety issues
- PK data so far continues to support once-daily dosing





Single Agent TGR-1202 Pharmacokinetics

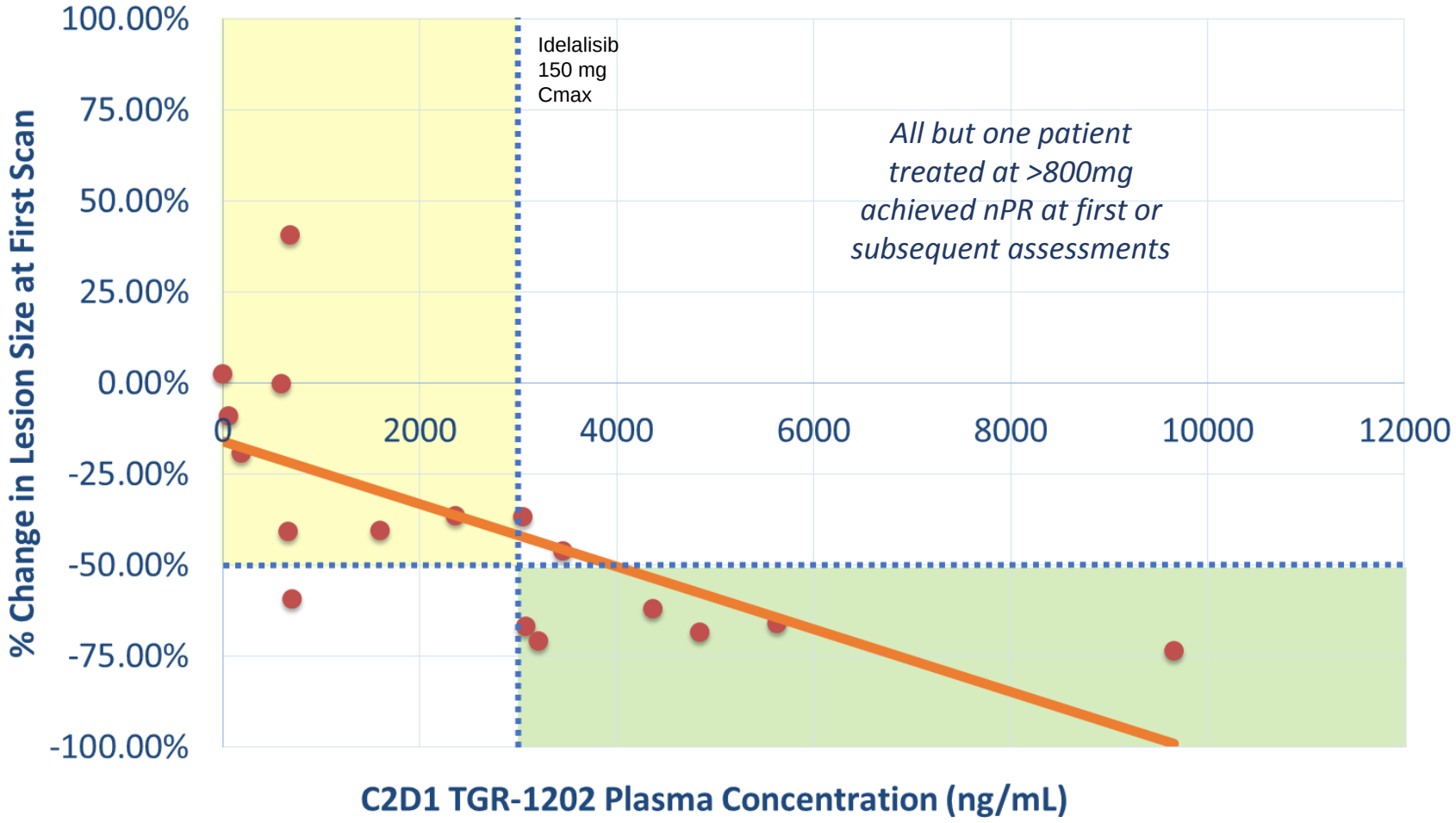
Initial Formulation (Fasting) vs. Micronized Formulation (Fed State)



Burris et al, ASH 2014

Single Agent TGR-1202 Exposure Response Relationship in CLL

Pre-Dose Plasma Concentration (Day 30) vs. First Scan Measurement (Day 60)

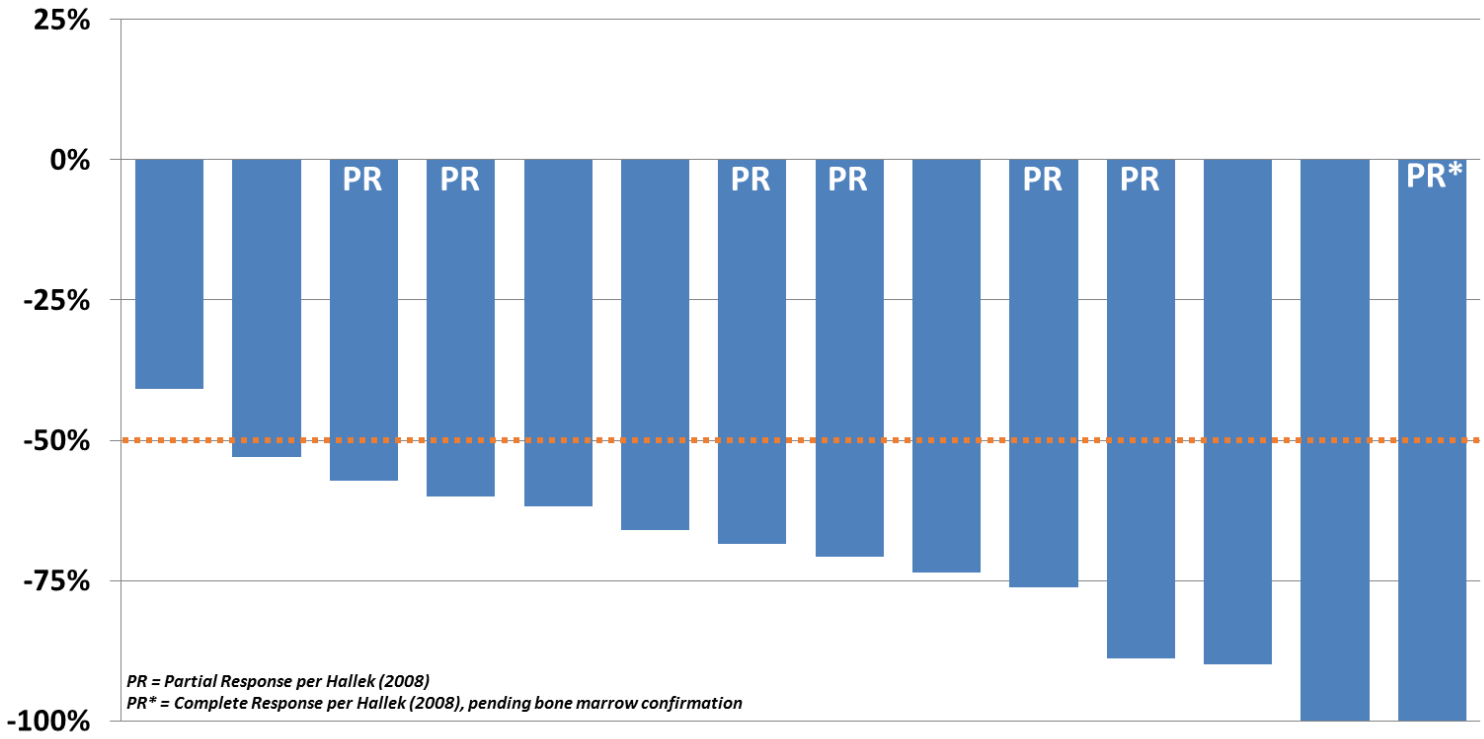


Burris et al, ASH 2014

Single Agent TGR-1202 Efficacy in CLL

Best Percent Change from Baseline in Nodal Size

Evaluable CLL Patients Treated at ≥800 mg of Initial Formulation or any Dose of Micronized Formulation



- 93% of CLL patients (13/14) treated at 800mg or higher achieved a nodal PR (median nodal reduction of 70%)
- Nodal reductions have been shown to improve with time on TGR-1202

Burris et al, ASH 2014

TGR-1202 - Safety

All Events (All Causality) in >10% (n=55)				
	All Grades		Grade 3/4	
	Events	%	Events	%
Diarrhea	17	31%	1	2%
Nausea	16	29%	-	-
Fatigue	14	25%	-	-
Cough	13	24%	-	-
Anorexia	11	20%	-	-
Headache	10	18%	-	-
Vomiting	10	18%	-	-
Rash	9	16%	2	4%
Neutropenia	8	15%	7	13%
Constipation	6	11%	-	-
Dyspnea	6	11%	2	4%
Thrombocytopenia	6	11%	4	7%

- No drug related hepatotoxicity, colitis, or pneumonitis observed to date
- Only 2 patients (< 4%) have come off study due to an adverse event (one unrelated, one possibly related)

Burris et al, ASH 2014

Room for Improvement…

Idelalisib Prescribing Information

July 2014

"Avoid concurrent use of Zydelig with other drugs that may cause liver toxicity.
Monitor ALT and AST in all patients every 2 weeks for the first 3 months of treatment, every 4 weeks for the next 3 months, then every 1 to 3 months thereafter.
Monitor weekly for liver toxicity if the ALT or AST rises above 3 times the upper limit of normal until resolved…"

WARNING: FATAL AND SERIOUS TOXICITIES: HEPATIC, SEVERE DIARRHEA, COLITIS, PNEUMONITIS, and INTESTINAL PERFORATION

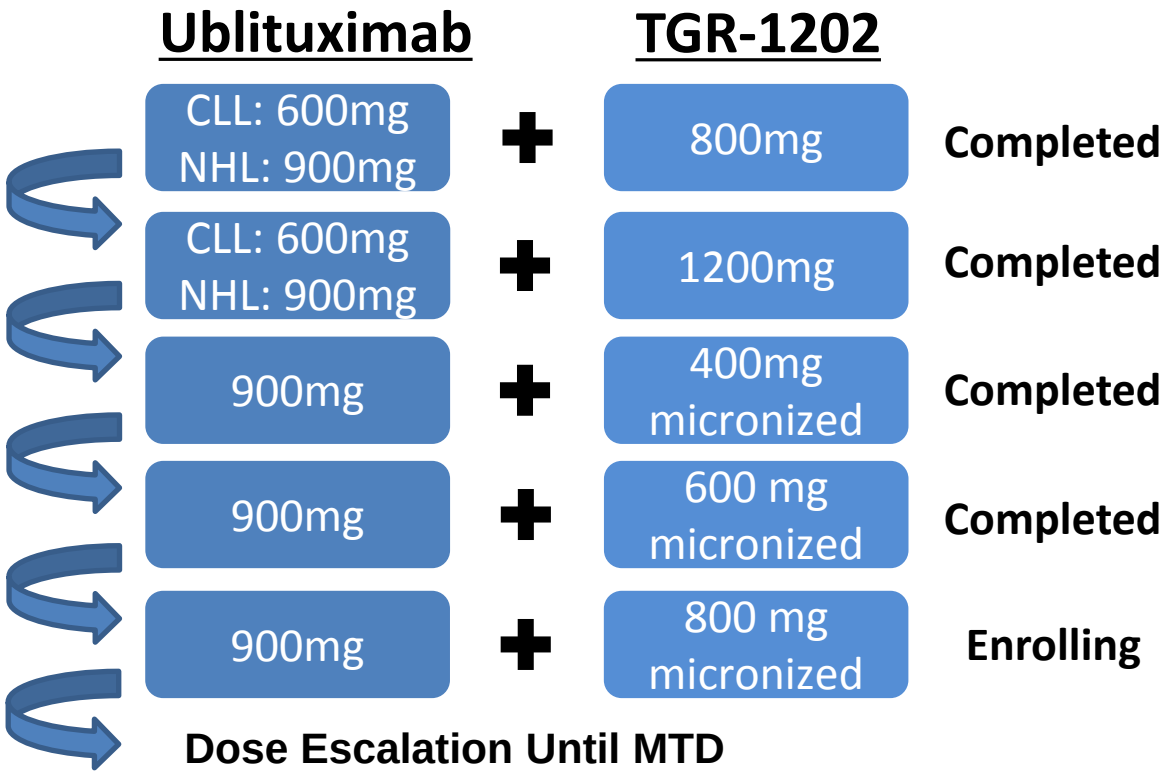
See full prescribing information for complete boxed warning.

- **Fatal and/or serious hepatotoxicity occurred in 14% of Zydelig-treated patients. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue Zydelig. (5.1)**
- **Fatal and/or serious and severe diarrhea or colitis occurred in 14% of Zydelig-treated patients. Monitor for the development of severe diarrhea or colitis. Interrupt and then reduce or discontinue Zydelig. (5.2)**
- **Fatal and serious pneumonitis can occur in Zydelig-treated patients. Monitor for pulmonary symptoms and bilateral interstitial infiltrates. Interrupt or discontinue Zydelig. (5.3)**
- **Fatal and serious intestinal perforation can occur in Zydelig-treated patients across clinical trials. Discontinue Zydelig if intestinal perforation is suspected. (5.4)**

Clinical Trials in Chronic Lymphocytic Leukemia
Serious adverse reactions were reported in 54 (49%) subjects treated with Zydelig + rituximab

Clinical Trials in Non-Hodgkin's Lymphoma
Adverse reactions resulted in **interruption or discontinuation for 78 (53%)** subjects

Trial Design/Demographics
TGR-1202 + Ublituximab



- Enrolling B-cell NHL and CLL/SLL
- No limit on prior therapies, incl. prior BTK and/or PI3K

- 67% of CLL had 17p and/or 11q del
- Median Prior Tx in FL: 5 (range 1 – 9)
- 5/7 DLBCL with Germinal Center (GCB)

Safety: TGR-1202 + Ublituximab

Adverse Events in ≥10%

(All Causality) n=27

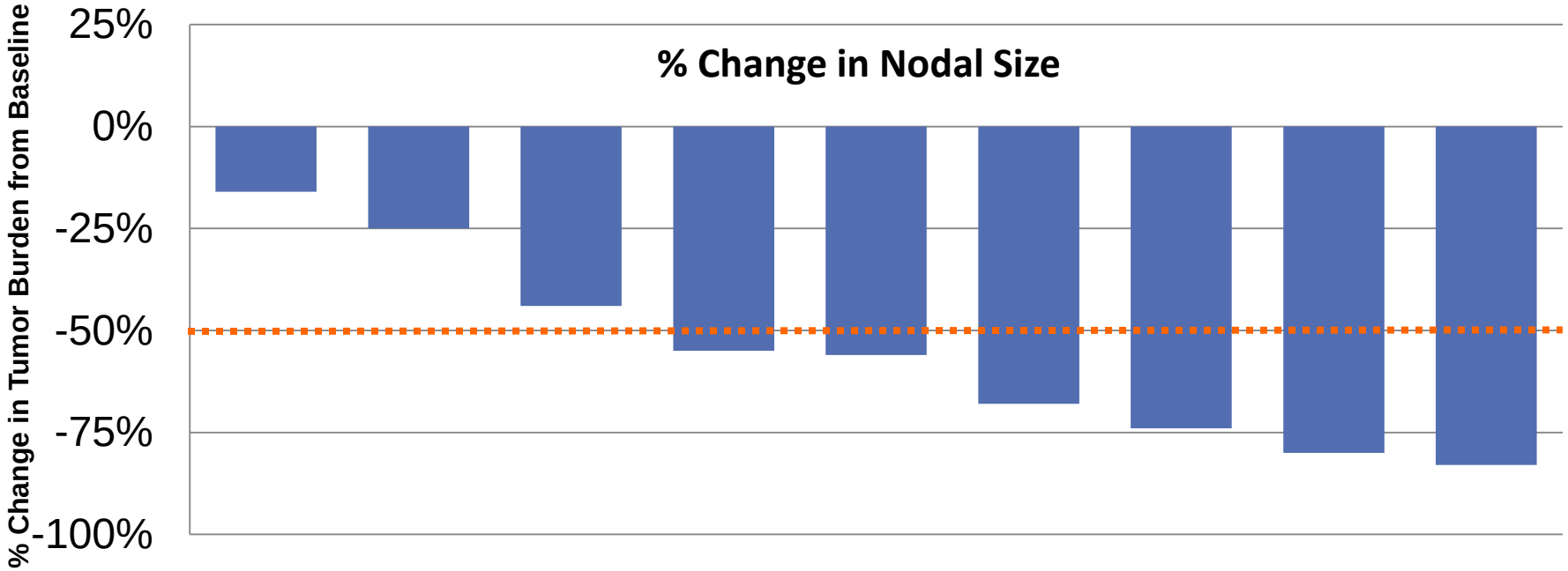
Adverse Event	All Grades n (%)	Grade 3/4 n (%)
Infusion reaction	14 (52)	1 (4)
Neutropenia	11 (41)	9 (33)
Nausea	10 (37)	-
Diarrhea	9 (33)	-
Fatigue	8 (30)	-
Insomnia	8 (30)	-
Dyspnea	6 (22)	1 (4)
Cough	5 (19)	-
Back Pain	4 (15)	-
Constipation	4 (15)	-
Sinusitis	4 (15)	-
Vomiting	4 (15)	-
Abdominal Pain	3 (11)	1 (4)
Fever	3 (11)	2 (7)
Upper Resp Inf	3 (11)	-

Lunning et al, ASH 2014

Activity in CLL/SLL: TGR-1202 + Ublituximab

Interim Data From Early Dose Escalation Cohorts

(Does not include patients at ≥600mg micronized)

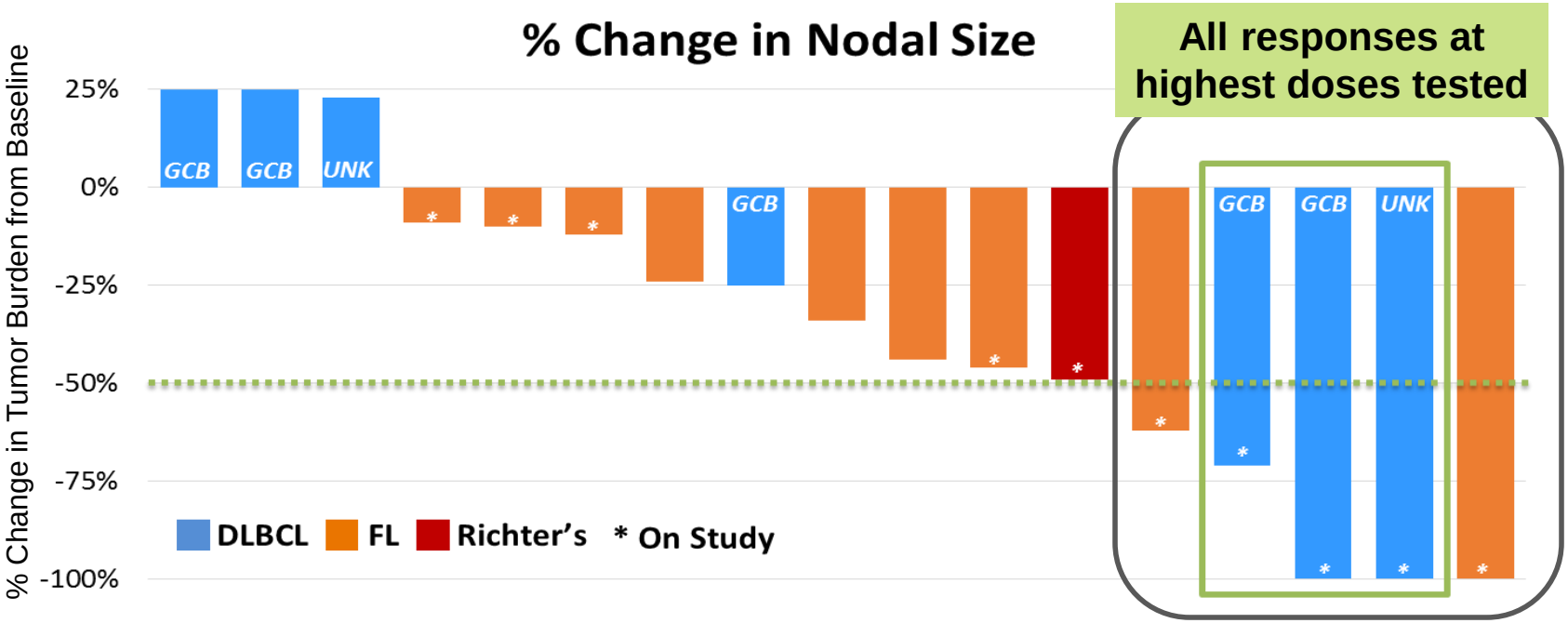


- 67% PR rate iwCLL (Hallek 2008)
- 6/9 patients with 17p and/or 11q
- **All CLL patients remain on study (3+ to 9+ months)**

Lunning et al, ASH 2014

Activity in NHL: TGR-1202 + Ublituximab

Interim Data From Early Dose Escalation Cohorts



- FL: 1 PET(-) CR and 1 PR
  - **78% of FL (N=9) patients have not progressed on study**
- DLBCL: **ORR 43% (3/7);**
  - **2 CR's confirmed by independent radiologic review**
  - **Responders remain on study > 7 months**

Lunning et al, ASH 2014

"Triplet": TGR-1202 + Ublituximab + Ibrutinib

- Initial cohorts for both NHL and CLL (n=5)

Ublituximab		TGR-1202		Ibrutinib
900mg	+	400 mg micronized	+	CLL: 420mg NHL: 560mg

- Safety: All Grade 1/2 AEs (no Grade 3/4 events to date)

Clinical Response at First Assessment (8 Weeks)

Histology	Description	Prior # Rx	Prior Ibrutinib	Rel/Ref	Rituximab Refractory	Response	% ↓
Follicular	Stage IV	4	Refractory	Refractory	Yes	PR	74%
MCL	Advanced	2	No	rAuto txp	No	CR	PET -
Richter's	17p	3	No	Refractory	Yes	PD	N/A
CLL	17p	2	No	Refractory	Yes	Too Early	N/A
Follicular	Stage IV	1	No	Refractory	Refractory	Too Early	N/A

Lunning et al, ASH 2014

2014 Milestones *(as presented at JPM)*

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

2015 Milestones

Q1 2015	Commence Phase 3 trial of TG-1101 plus Ibrutinib in High-Risk CLL
1H 2015	Initiate 2nd Phase 3 clinical trial
1H 2015	Present updated clinical data at ASCO, EHA & Lugano
2H 2015	Initiate at least one additional triple therapy clinical trial
2H 2015	Initiate first clinical trial in Autoimmune Diseases
2H 2015	Advance IRAK-4 inhibitor program into the clinic
2H 2015	Initiate a 3rd Phase 3 clinical trial
Q4 2015	Present updated clinical data at ASH 2015

Corporate & Financial

Key Financial Statistics	
Ticker:	**TGTX (NasdaqCM)**
Price:	**$14.98 (close as of January 14, 2014)**
Shares:	**~44M (Primary); ~48M (fully-diluted)**
Cash:	**~$93.4M (pro forma as of September 30, 2014)**
Burn:	**$4-$6M per quarter**
Time:	**2+ years of cash**

Key Takeaways

- TG-1101 Phase 3 in Combination with ibrutinib
  - High probability of success, supported by strong Phase 2 data
  - Conducted pursuant to SPA
  - Very attractive regimen: tolerability and efficacy
- Proprietary combination entering Phase 3 in 2015
  - Safety and efficacy profile at higher doses could be best-in-class combination across CLL and NHL
  - Pricing leverage
- Additional upside in autoimmune diseases and leadership in next generation triple therapy
  - BTK underway, IRAK4 before YE, others?

TG Therapeutics

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