TG Therapeutics

NASDAQ: TGTX

J.P. Morgan Healthcare Conference

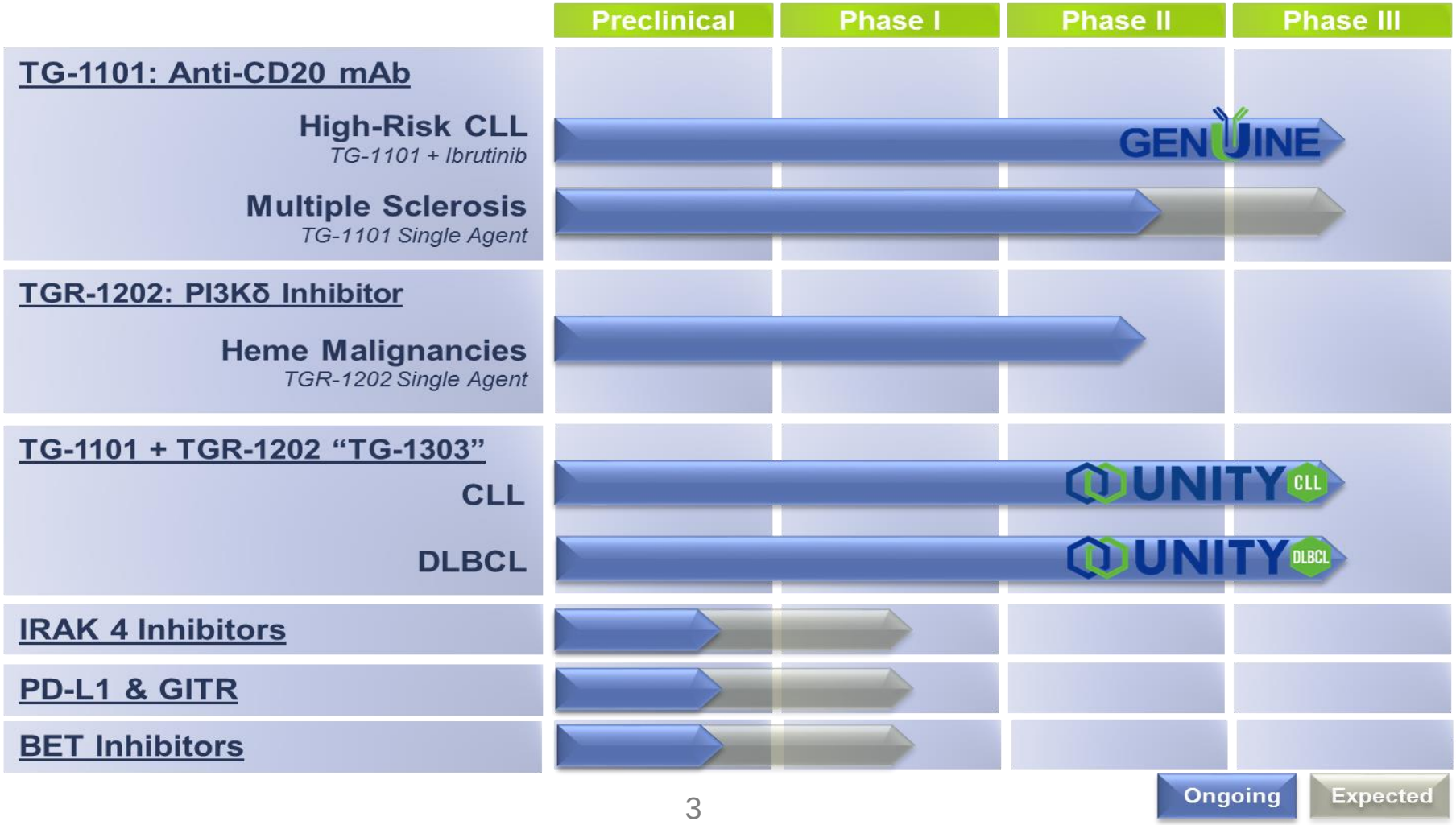
January 2017

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.

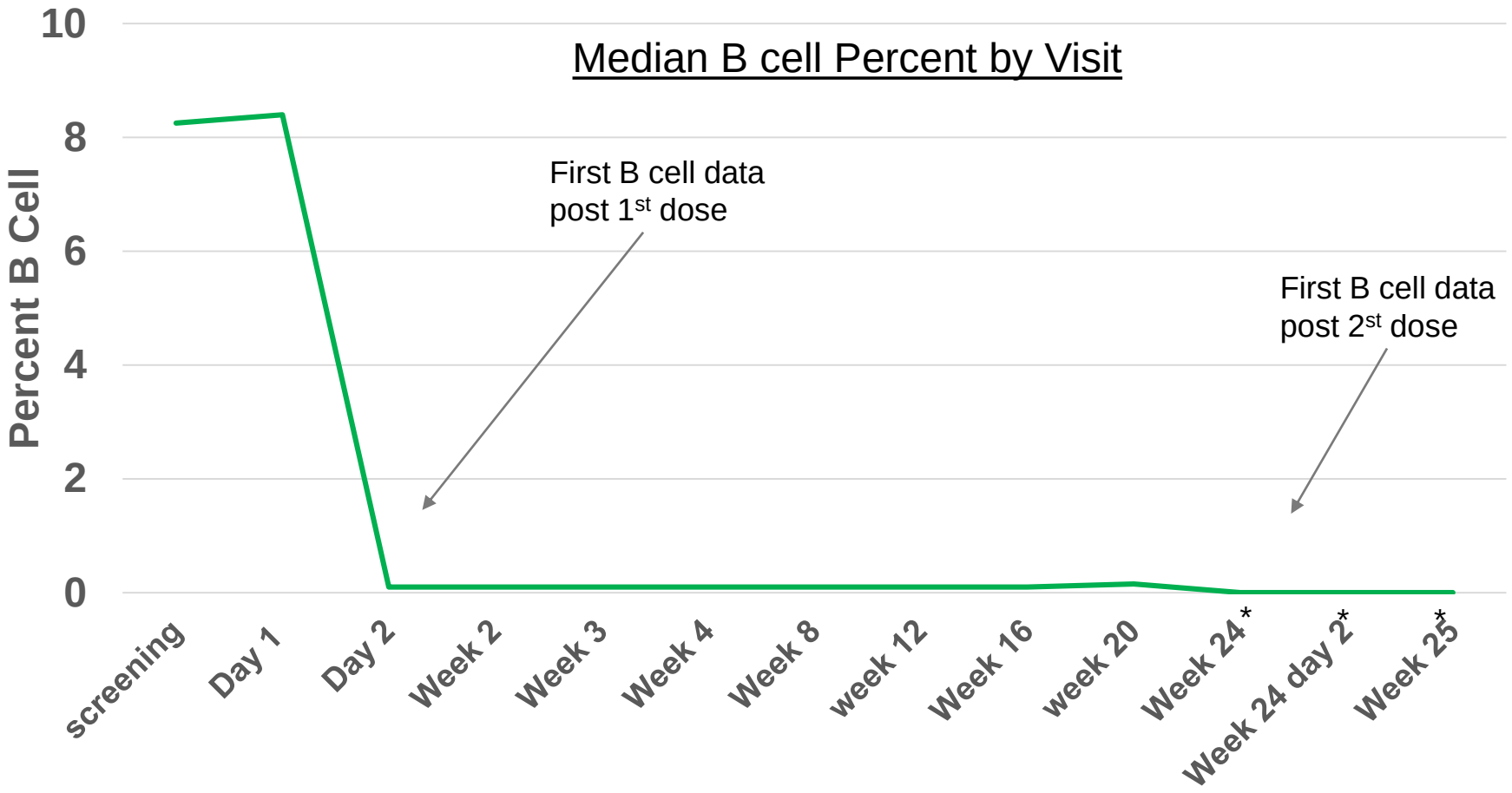
TG Therapeutics, Inc.

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



MS Phase 2– Key Findings

- Median B-cell depletion: 99%
- One hour infusion was well tolerated



* Note: only one subject has reached week 24 and beyond

Anti-CD20 mAbs in MS

Phase III Studies of Ocrelizumab ("Ocre") in RMS

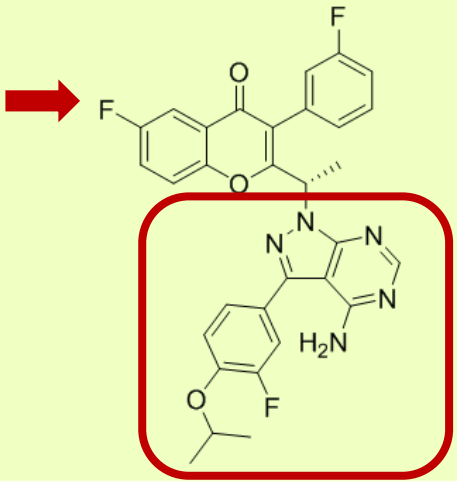
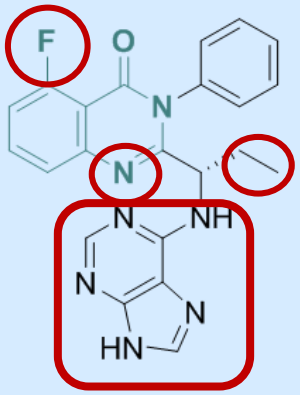
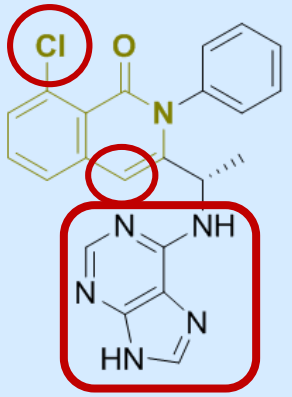
mAb	ARR by Y2 (Primary Endpoint)	Reduction in Total Gd Lesions (Secondary Endpoint)	Reduction in New Gd Lesions (Secondary Endpoint)
OPERA I OCRE 600mg v. Rebif N=822	-46% ARR (P<0.0001)	-94% (P<0.0001)	-77% (P<0.0001)
OPERA II OCRE 600mg v. Rebif N=835	-47% ARR (P<0.0001)	-95% (P<0.0001)	-83% (P<0.0001)

Opera I and II were identically designed studies conducted in US and EU

<u>TG-1101 MS Program Update:</u>

- Phase 2 underway, enrollment complete in Part 1
- Phase 3 under development, seeking guidance from FDA on design

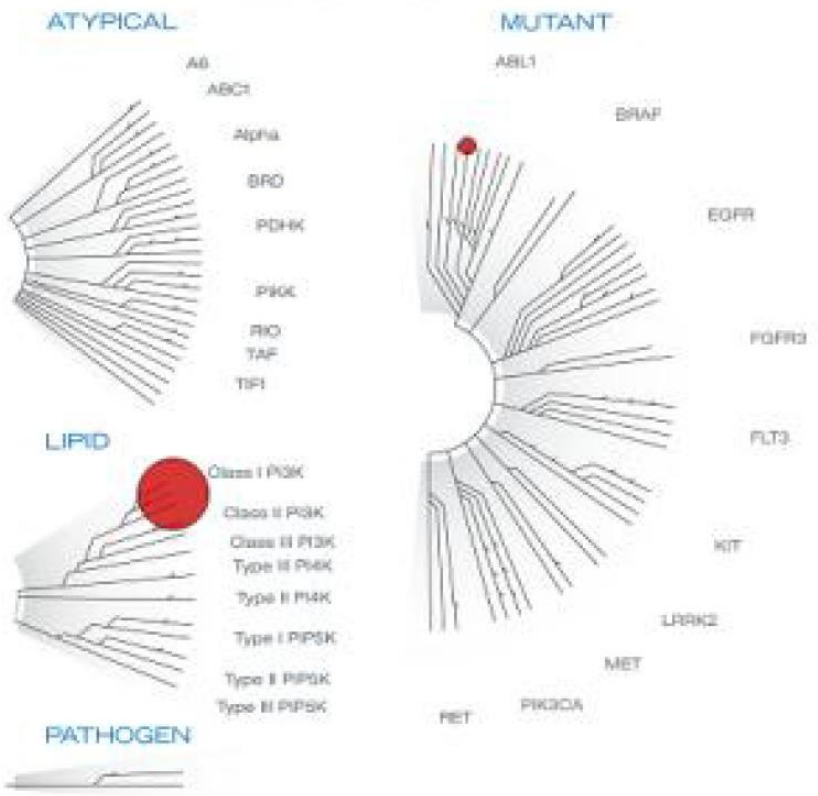
TGR-1202: Novel PI3K delta Inhibitor

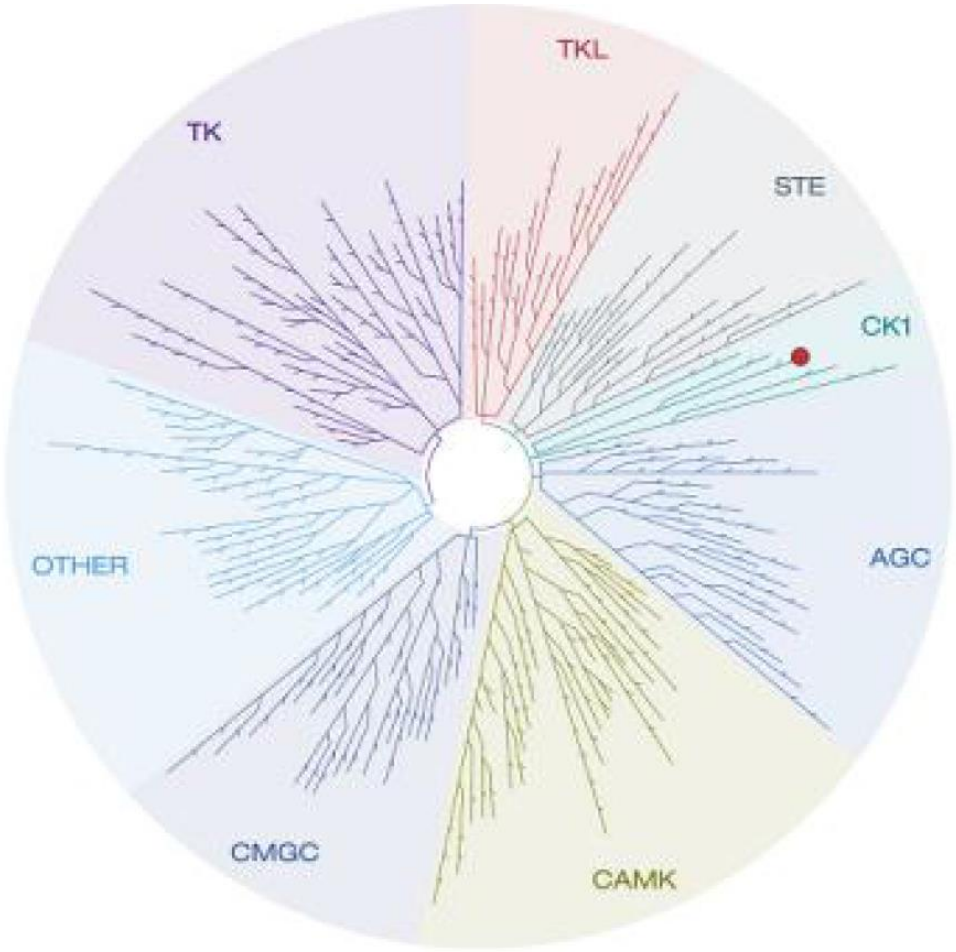
TGR-1202	Idelalisib (GS-1101)	Duvelisib (IPI-145)
		
Delta	Delta	Delta/Gamma
QD	BID	BID

- Significant structural differences compared to other PI3Kδ
- PK profile that allows once-daily oral dosing

Burris et al, ASCO 2015, Abstract # 7069

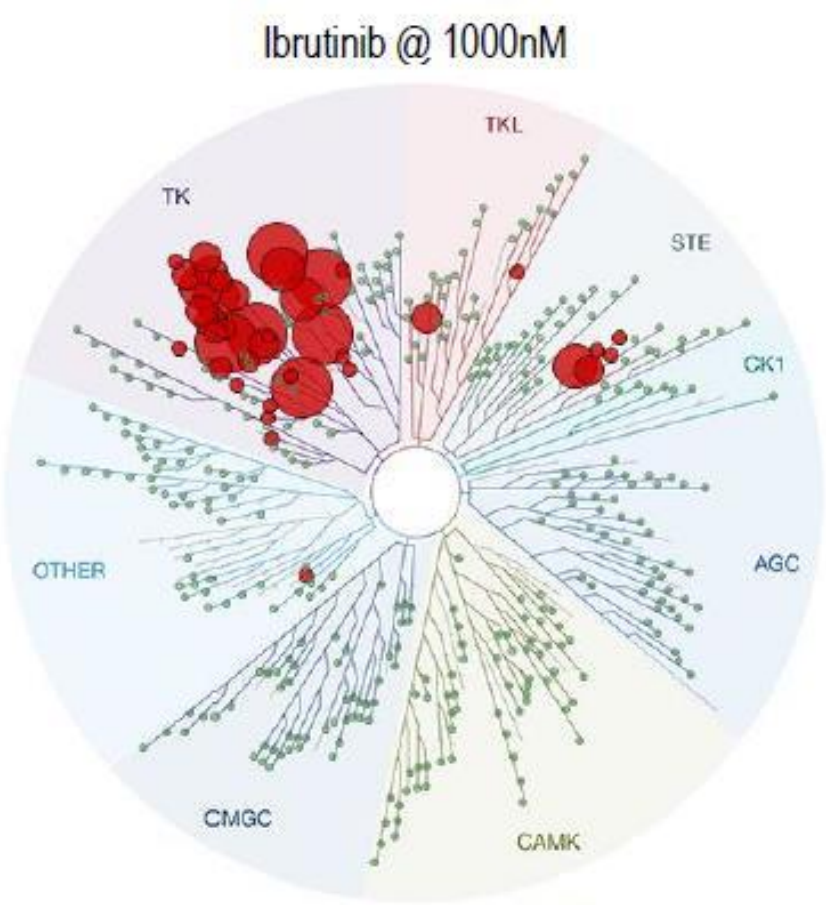
TGR-1202 Selectivity

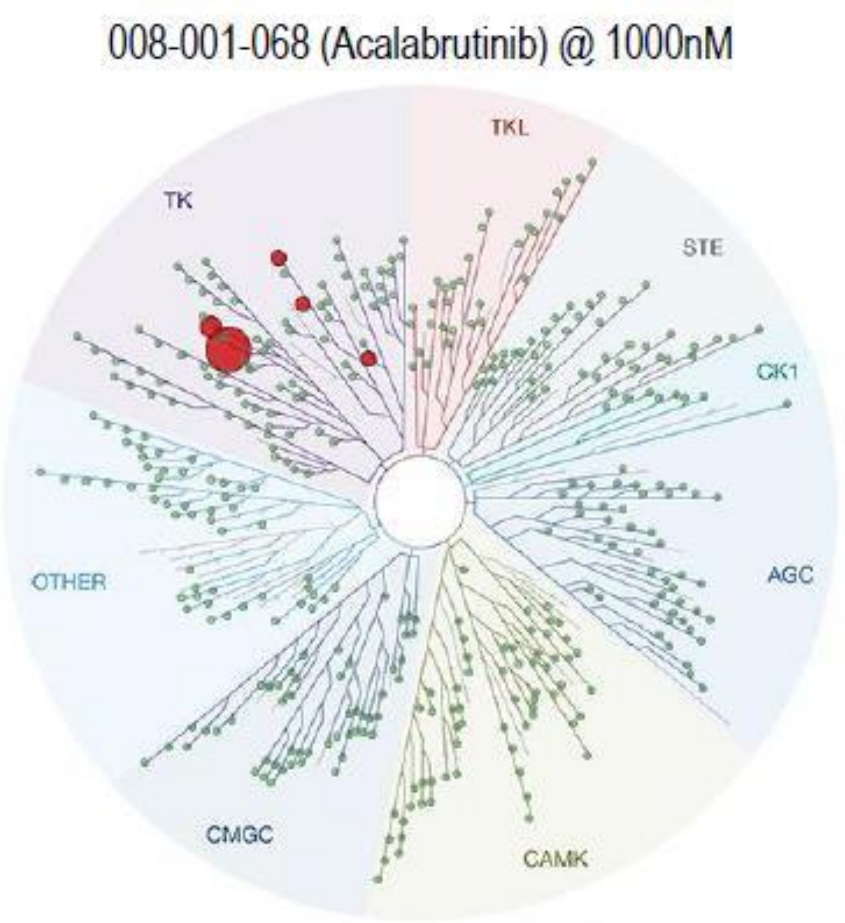




DiscoverRx Kinome Scan against a panel of 442 kinases

BTK Selectivity

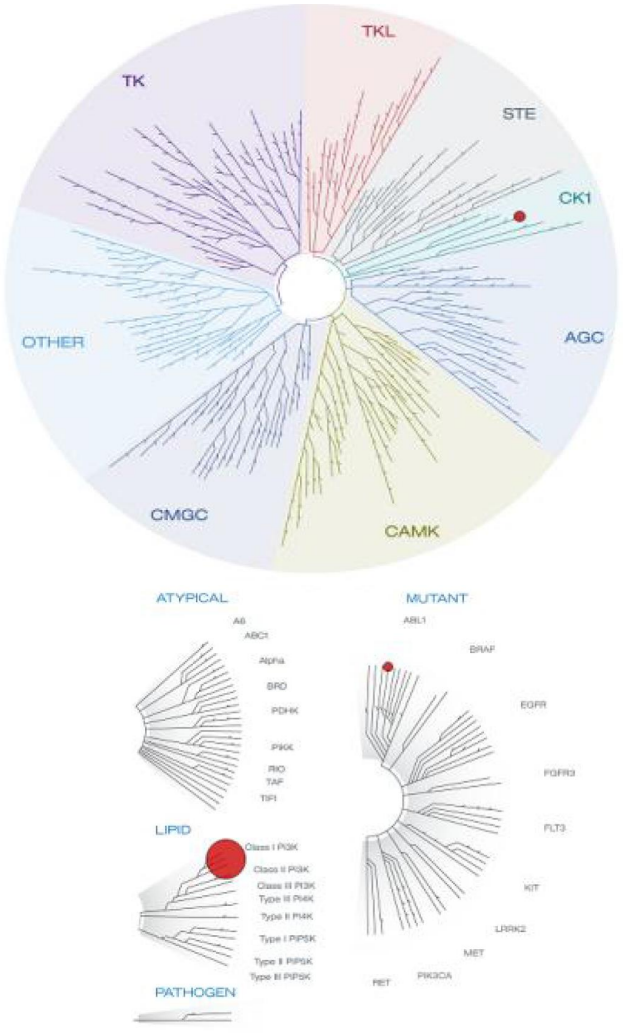




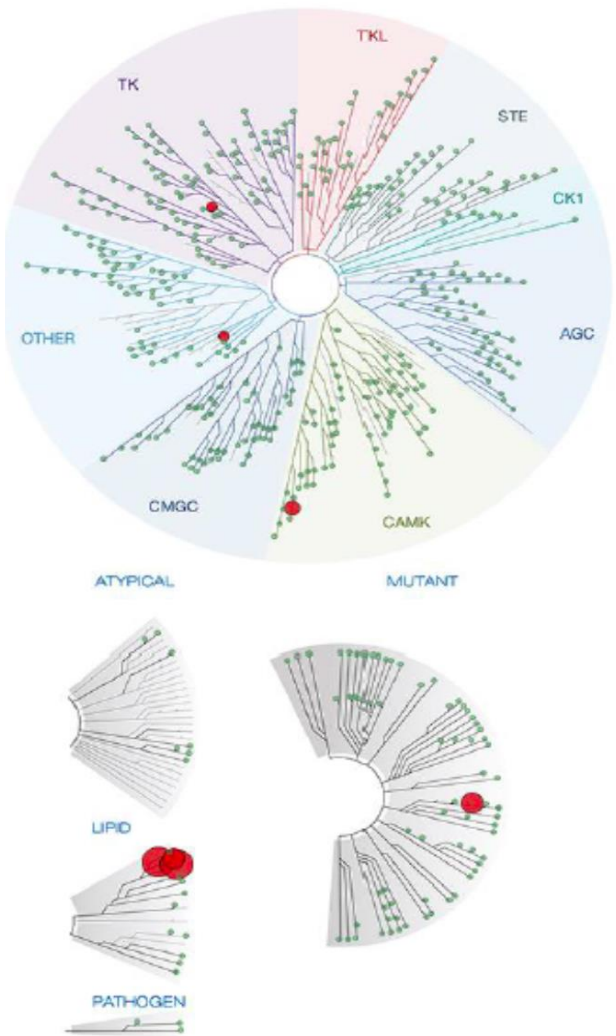
DiscoverRx Kinome Scan against a panel of 442 kinases

Other PI3K-Delta Selectivity

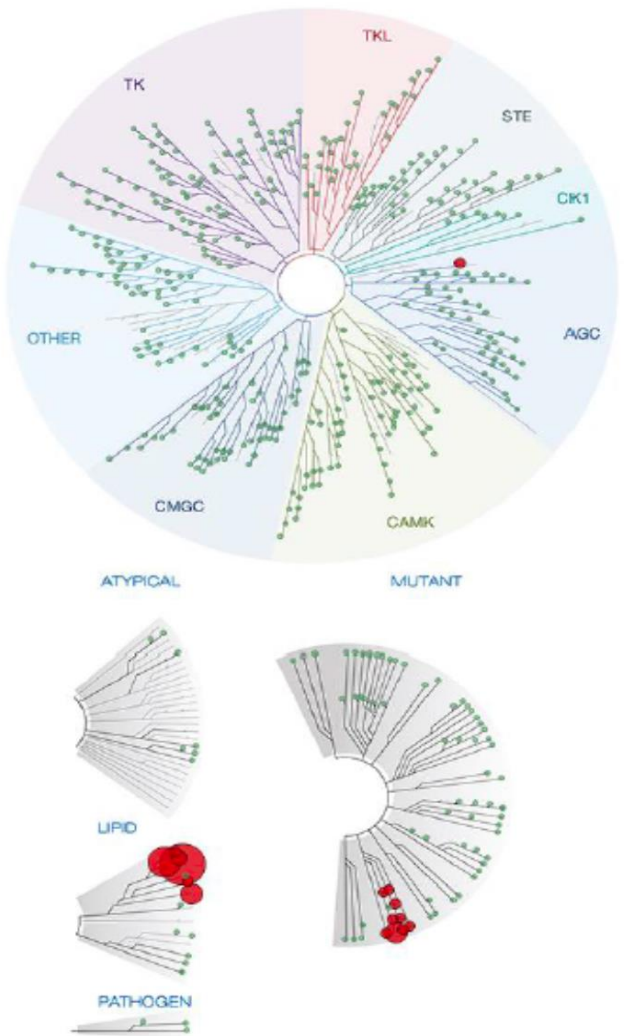
TGR-1202 @ 1000nM



CAL-101 (Idelalisib, GS-1101) @ 1000nM



Duvelisib (IPI-145, INK1197) @ 1000nM



DiscoverRx Kinome Scan against a panel of 442 kinases

What does the basic science teach us?

Author	Model	Relevant Findings
Okkenhaug, et. al Science 2002	KI Delta model	All other organs appeared to be normal, except mice developed a mild inflammatory bowel disease
Jou, et. al. Molecular and Cell Biology 2002	KO Delta model	Did not observe an inflammatory bowel disease in mice
Uno, et. al. Gastroenterology November 2010	Double KI Delta – KO IL10	A mild spontaneous colitis was demonstrated in Delta KI mouse. Double KI-KO mice developed severe colitis.
Kaneda, et. al Nature November 2016	Role of Gamma	Macrophages lacking PI3Kγ activity induced pro-inflammatory cytokines such as IL12 with a concomitant reduction in IL10
Okkenhaug, et. al Blood 2007	Double KI/KO Delta –Gamma	Mice lacking PI3Kγ and PI3Kδ function developed eosinophilic inflammation in multiple mucosal organs

Idelalisib Caused Rapid and Serious Liver Toxicity in Front-Line Patients

CLINICAL TRIALS AND OBSERVATIONS

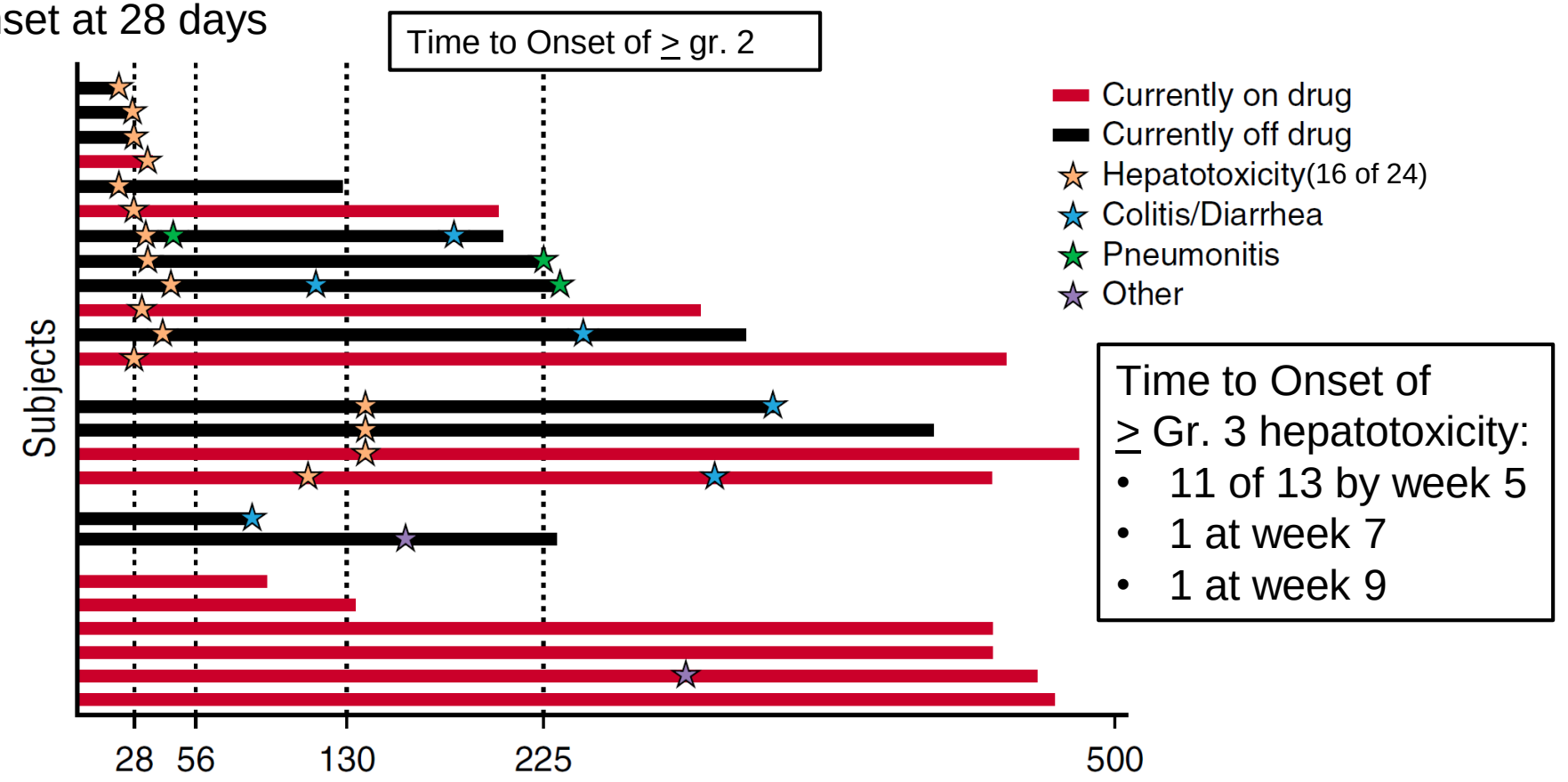
Idelalisib given front-line for treatment of chronic lymphocytic leukemia causes frequent immune-mediated hepatotoxicity

Benjamin L. Lampson, Jennifer R. Brown, et.al.

BLOOD, 14 JULY 2016 x VOLUME 128, NUMBER 2

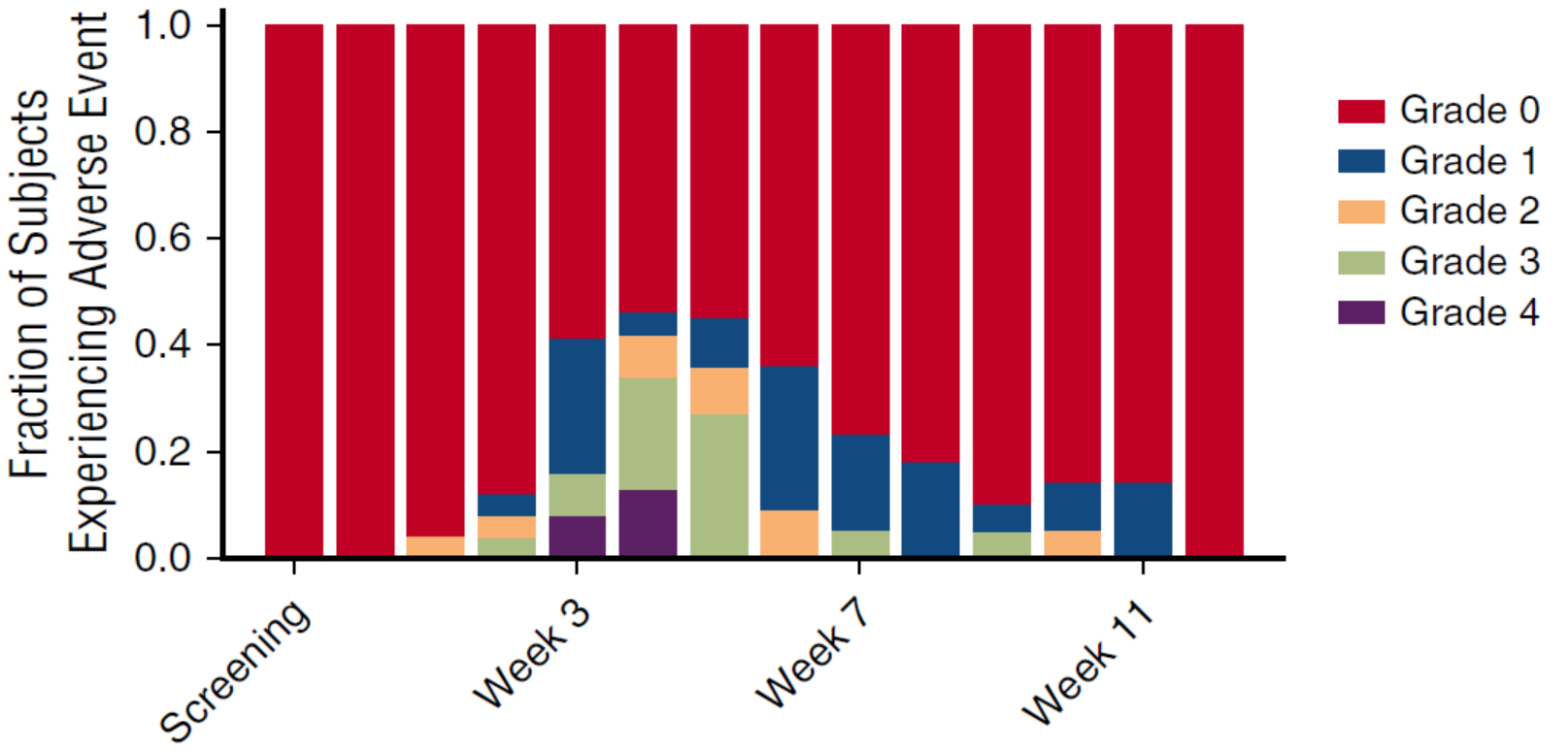
Idelalisib Related Hepatotoxicity

- Brown et al reported high rates of immune-mediated hepatotoxicity in patients with front-line CLL treated with idelalisib
- Decreases in Treg population implicated
- Transaminitis rates of 79% all grades (gr.3/4 of 54% (13 of 24)), with median onset at 28 days



Lampson, Brown et al, Blood 2016

Idelalisib Liver Tox in Front-line Patients



- Almost all Gr. 3/4 liver tox for idelalisib was observed by week 5
  - Gr. 3/4 Liver Tox at 6 weeks 46% (11/24 patients)
  - All Grades Liver Tox at 6 weeks 79% (19/24 patients)

Lampson, Brown et al, Blood 2016

Idelalisib Label

“Limitation of use: Zydelig is not indicated and is not recommended for first-line treatment of any patient”

First UNITY-CLL DSMB on November 21, 2016

- UNITY-CLL is enrolling front-line and previously treated patients with CLL

- As of DSMB meeting, there were a comparable number of front-line patients on study for comparable timeframe as the Jennifer Brown study

"The DSMB did not find any safety concerns and recommended the study continue without modification"

Phase 3 Clinical Trial
TG-1101 + TGR-1202 ("TG-1303")

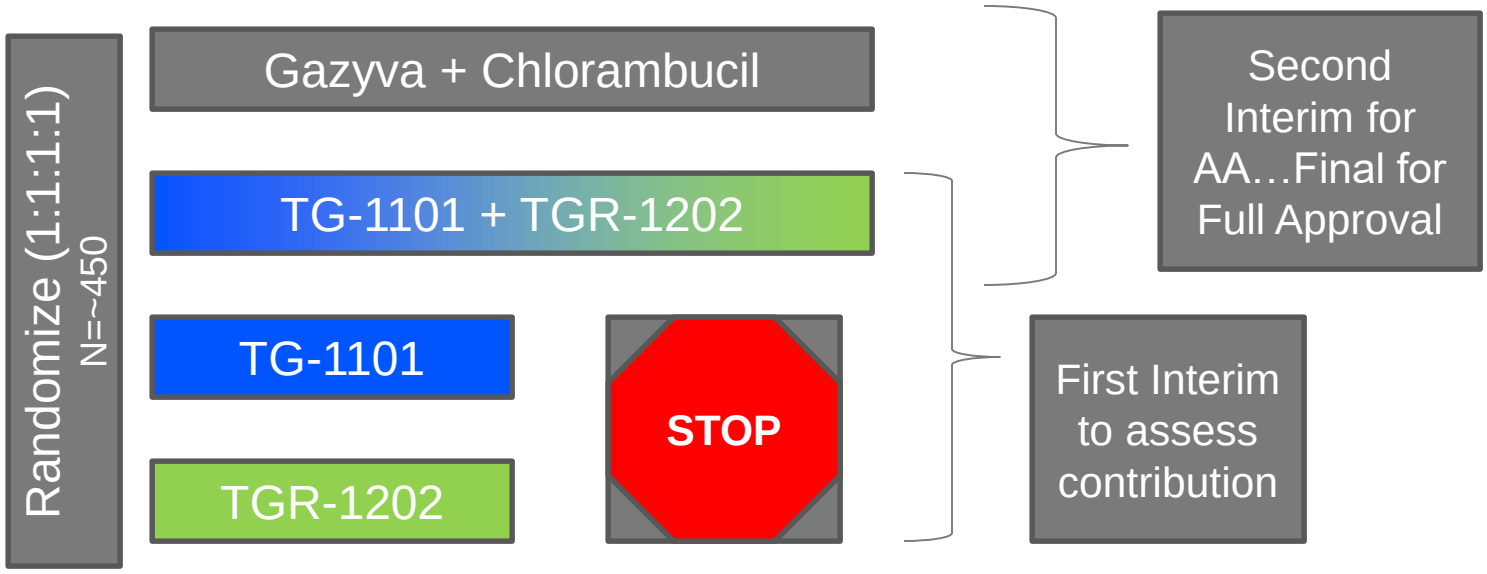
UNITY CLL

TG THERAPEUTICS

GLYCOENGINEERED UBLITUXIMAB + PI3K DELTA TGR-1202

PHASE 3 TRIAL IN CLL

*Conducted pursuant to SPA



UNITY-CLL Study Update

- Site Status:
  - ~100 sites for UNITY-CLL open to date in US
  - Ex-US sites opening bringing total expected to 150+
  - By end of March should have nearly all sites open globally

- Enrollment Update:
  - **~140 randomized** patients at December 31, 2016
  - **Enrolled ~25 patients** in December 2016
  - Expect to conduct interim analysis to eliminate arms mid-year
  - On track for completing enrollment by **Q1 2018** (updating guidance from 1H18)

Is there a need for TGR-1202?

Most common ibrutinib related toxicities as reasons for discontinuation	
Relapsed CLL (%)	**Front-line CLL (%)**
Atrial fibrillation (12.3)	
Infection (10.7)	Arthralgia (41.6)
Pneumonitis (9.9)	Atrial fibrillation (25)
Bleeding (9)	Rash (16)
Diarrhea (6.6)	

Median times to ibrutinib discontinuation stratified by toxicity	
Bleeding	8 months
Diarrhea	7.5 months
Atrial fibrillation	7 months
Infection	6 months
Arthralgia	5 months
Pneumonitis	4.5 months
Rash	3.5 months

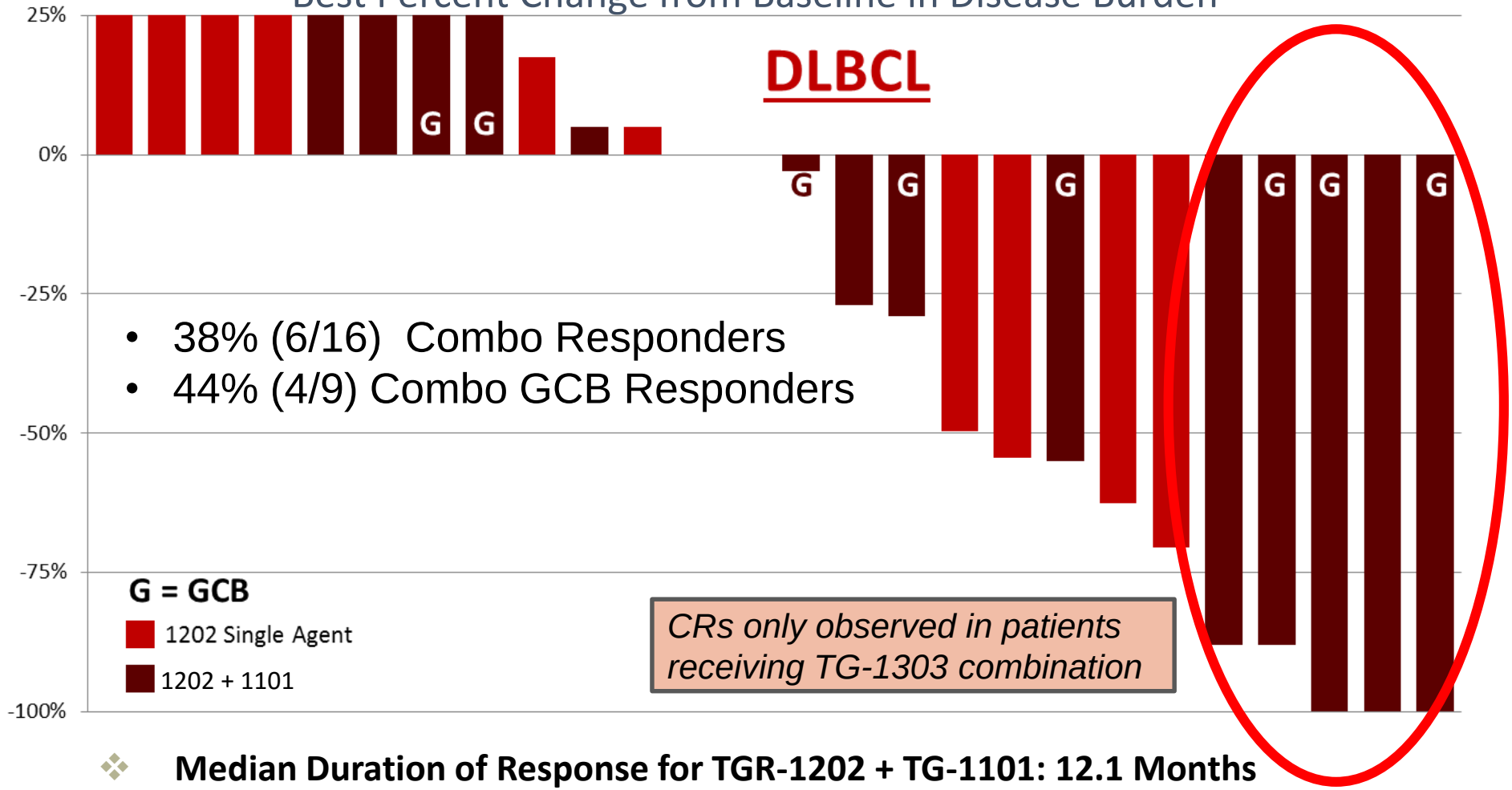
- ***In the largest reported series on ibrutinb treated CLL patients, 40% of patients have discontinued ibrutinib during this observation period.***
- Ibrutinib intolerance was the most common reason for discontinuation in all settings.
- **~20% of patients are ineligible for ibrutinib because of DDI, CV risk and bleeding risk**

Mato et al, ASH 2016

Integrated Analysis (TGR-1202 Monotherapy and TGR-1202 + TG-1101): DLBCL Efficacy

Patients Treated at "Higher Doses" of TGR-1202

Best Percent Change from Baseline in Disease Burden



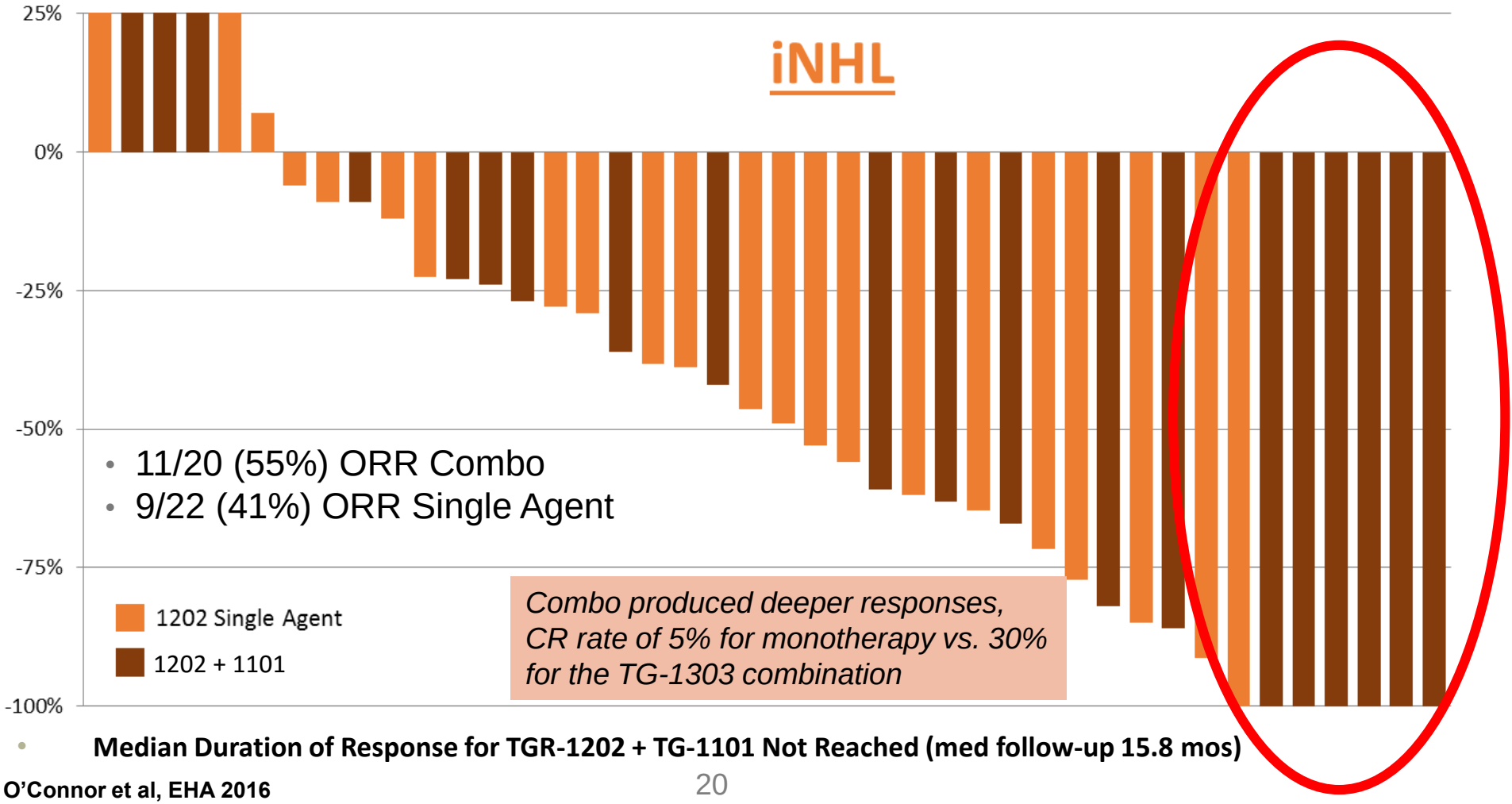
❖ **Median Duration of Response for TGR-1202 + TG-1101: 12.1 Months**

O'Connor et al, EHA 2016

Integrated Analysis (TGR-1202 Monotherapy and TGR-1202 + TG-1101): iNHL Efficacy

Patients Treated at "Higher Doses" of TGR-1202

Best Percent Change from Baseline in Disease Burden



- **Median Duration of Response for TGR-1202 + TG-1101 Not Reached (med follow-up 15.8 mos)**

O'Connor et al, EHA 2016

Recent Kite Data DLBCL

Kite Data
n=51

- ORR: 39%
- CR: 33%

at 3 months

- 2 deaths from treatment
- 29% Gr.3/4 Febrile neutropenia
- 34% Gr. 3/4 Neuro-tox
- 26% Gr. 3/4 Encephalopathy
- 18% Gr. 3/4 Cytokine Release Syndrome (CRS)

- *~50% of "responders" progressed btw months 2 and 3*

TG-1303
n=16

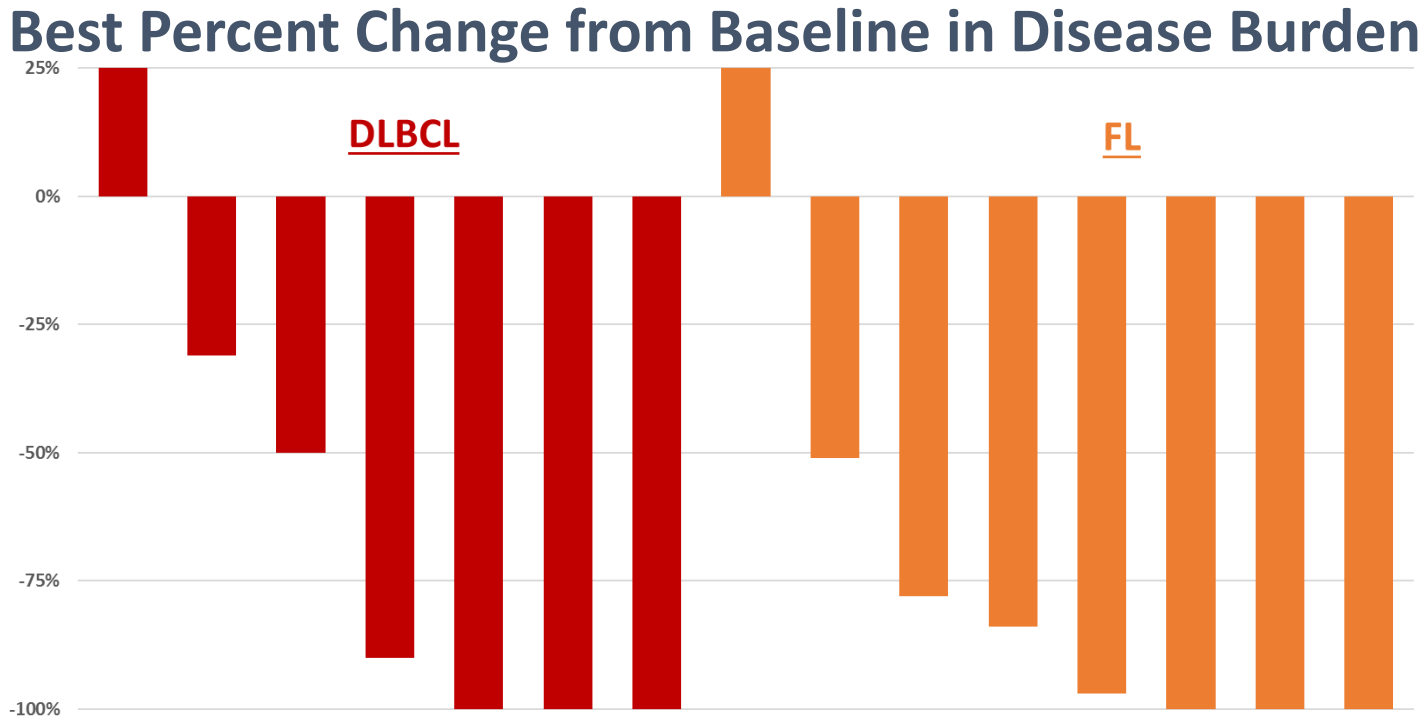
- ORR: 38%
- CR: 19%

at 3 months

- 0 deaths from treatment
- 0% Febrile neutropenia
- 0% Neuro-tox
- 0% Encephalopathy
- 0% Cytokine Release Syndrome (CRS)

- *Median Duration: 12.1 Months*

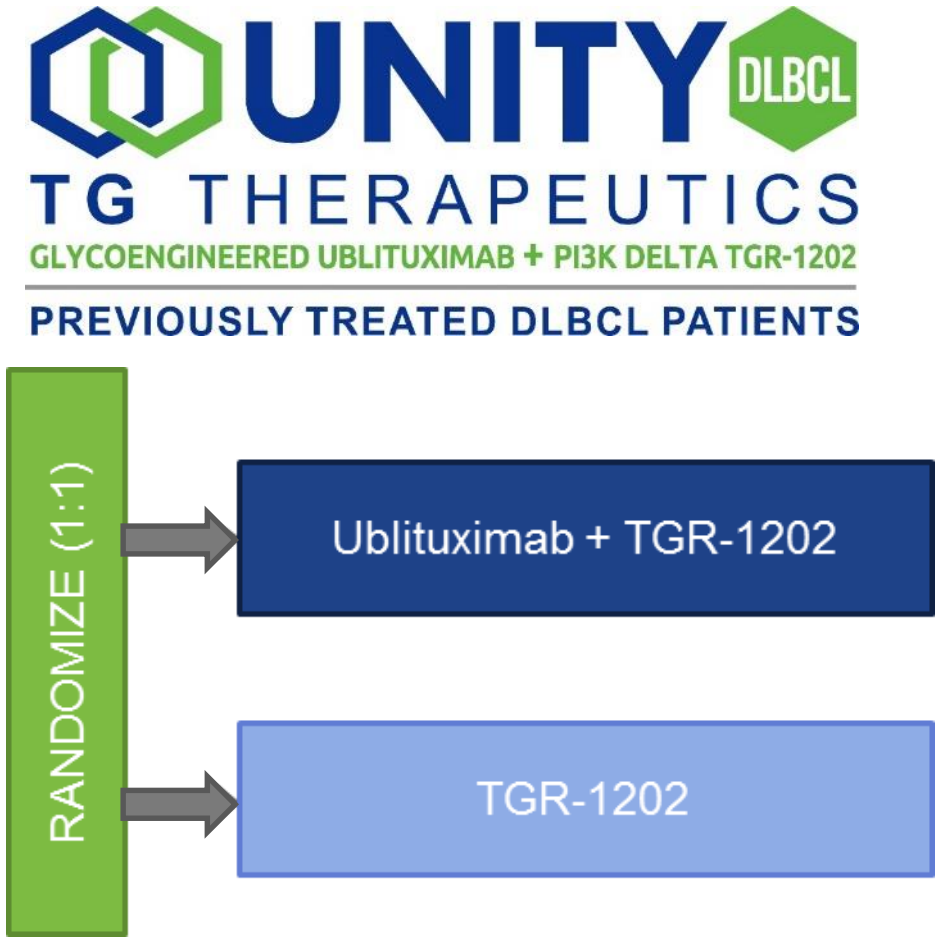
TG-1101 + TGR-1202 + Benda: Efficacy



Type	Pts (n)	CR (n)	PR (n)	ORR n (%)	SD (n)	PD (n)
DLBCL	7	3	2	**5 (71%)**	1	1
FL	8	3	4	**7 (88%)**	-	1
Total	**15**	**6**	**6**	**12 (80%)**	**1**	**2**

Lunning et al, ASH 2016

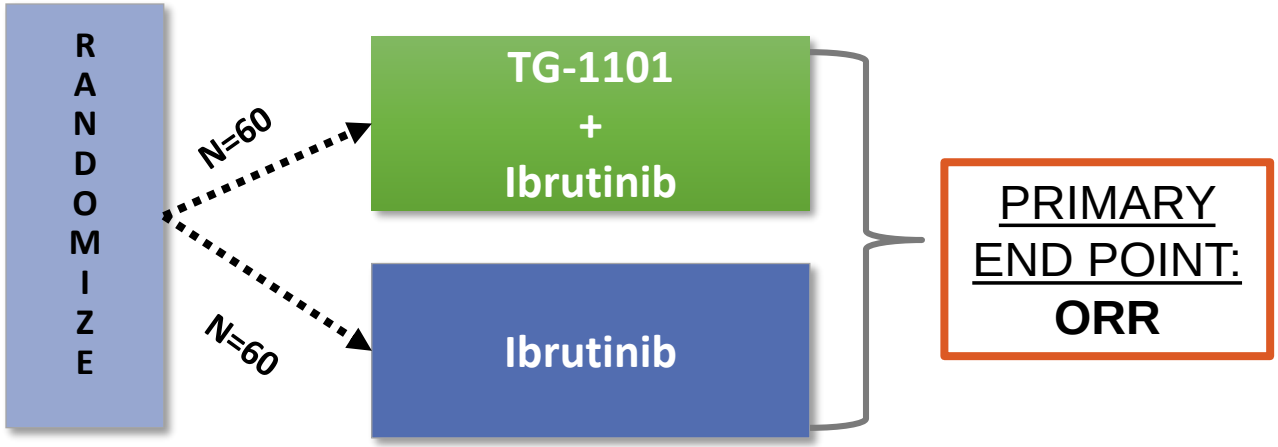
UNITY-DLBCL – Phase 2b
Registration Directed Trial



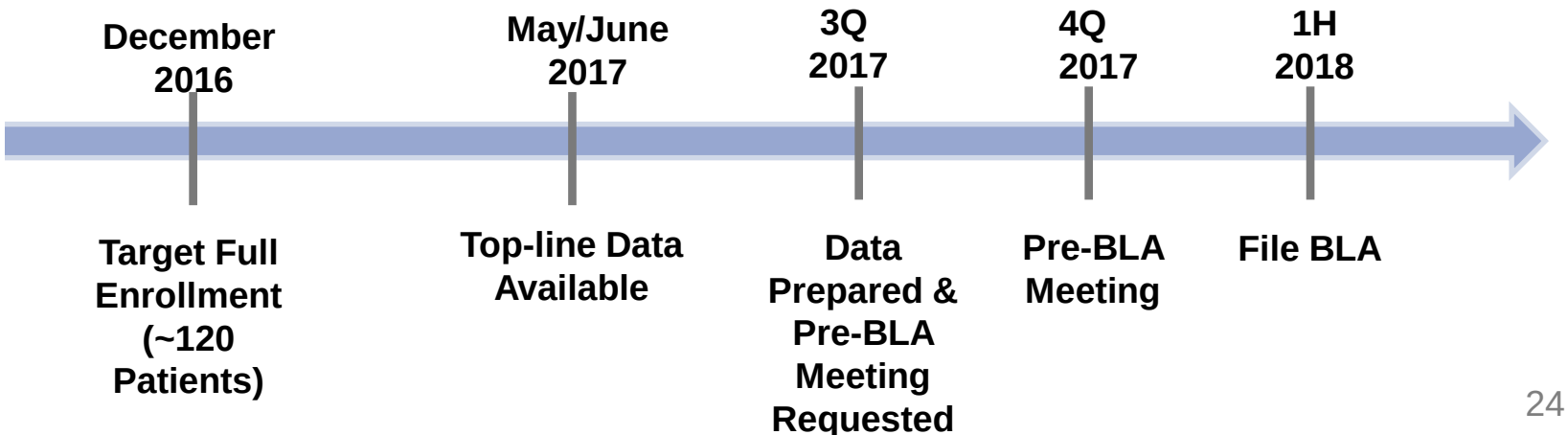
- Expect >50 sites to participate
- EU to open 1H 2017
- First Interim analysis expected mid-17
  - **Expectation to drop TGR-1202 as "Futile"**
  - **1303 arm to continue to ~100 patients**
  - **Replace TGR-1202 arm with 1303 + Benda**

Revised Phase 3 GENUINE Trial
For Potential Accelerated Approval

GENUINE
TG THERAPEUTICS
GLYCOENGINEERED UBLITUXIMAB + IBRUTINIB
PHASE 3 TRIAL IN HIGH-RISK CLL

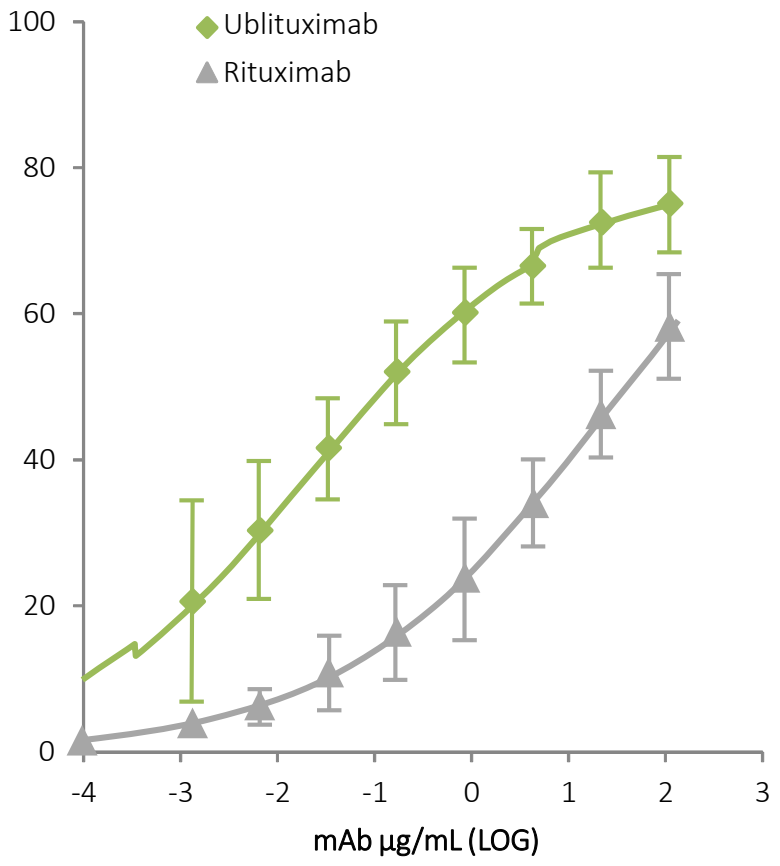


Registration Timeline



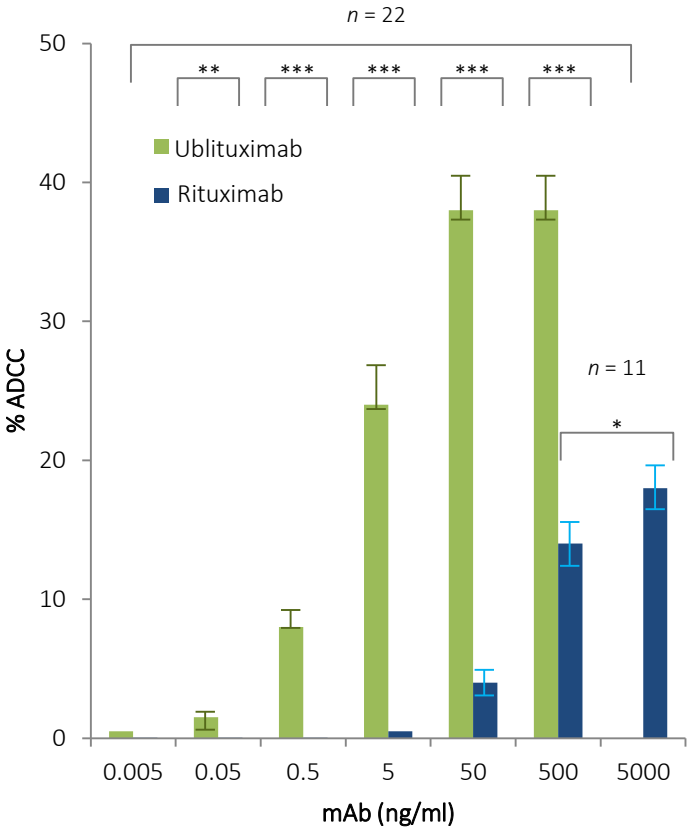
Superior B-Cell Depletion and Potency

Enhanced ADCC Activity Results in Superior *in vitro* B-Cell Depletion



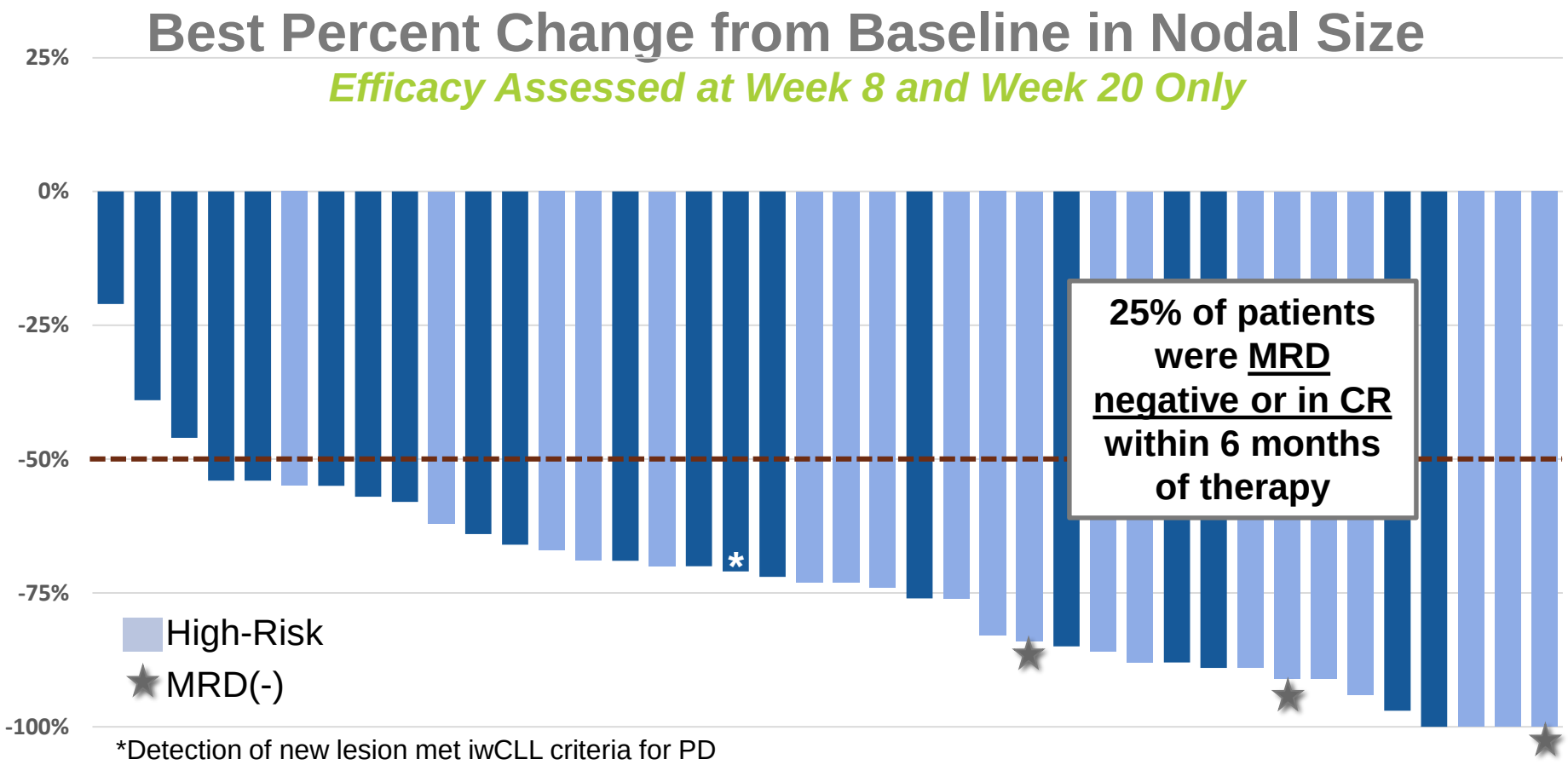
Ublituximab vs. Rituximab *ADCC Induction in CLL Patient Donor Cell Lines*

Published, peer reviewed pre-clinical data demonstrates equivalent ADCC levels using Ublituximab at 100 times less concentration of Rituximab



Source: Company, de Romeuf et al, 2008, Le Garff-Tavernier et al, 2011.

Phase II TG-1101 + Ibrutinib Efficacy: Nodal Reductions



- **88% ORR with 95% ORR in high risk patients**
- Well tolerated with few Gr. 3/4 events

Sharman, Burke et al, ICML 2015

GENUINE Control Arm
Historical ORR

Ibrutinib Single Agent ORR				
Study *(Ibrutinib Label)*	**Patient Population**	**n**	**Ibrutinib ORR**	**Median follow up time**
Study 1: Ibrutinib Open Label Multicenter trial	Previously treated CLL	48	58.3% *NO CR's	20.9 months * NEJM, Byrd 2013
Study 2: Randomized open label study of Ibrutinib v Ofatumumab (RESONATE)	Previously treated CLL	136	42.6% *NO CR's	9.4 months *NEJM, Byrd 2014
Study 2: RESONATE	17p only	63	47.6% *NO CR's	9.4 months *NEJM, Byrd 2014

Labeled Range – ORR Ibrutinib single agent:
~43% - 58.3%, with no CRs

Expected median follow-up for GENUINE Study: ~12 months

GENUINE Treatment Arm
Target ORR

Ibrutinib Combo Data per Label			
Study	**Patient Population**	**n**	**ORR**
ibrutinib plus bendamustine rituxan	Previously treated CLL or SLL	289	**82.7% (8.3% CR)**

Target ORR for GENUINE: 80-85% without Chemo

2017 Major Milestones

1H 2017	Topline data available for GENUINE Trial
1H 2017	Present data from Phase 2 MS trial at major medical meeting
1H 2017	Initiate MS Phase 3 Trial
1H 2017	Present updated clinical data at ASCO, EHA & Lugano
2H 2017	Decision on filing of GENUINE for Accelerated Approval
2H 2017	UNITY-CLL enrollment update & interim analysis of single agent arms
2H 2017	Present interim data from Phase 2b UNITY-DLBCL
2H 2017	Present updated clinical data at ASH 2017

Corporate & Financial

Key Financial Statistics

Ticker:	**TGTX (NasdaqCM)**
Price:	**$5.00 (close as of January 10, 2017)**
Shares:	**~55M (fully-diluted)**
Cash:	**~$60.7M (as of September 30, 2016)**
Runway:	**Into the first half of 2018**

TG Therapeutics

NASDAQ: TGTX