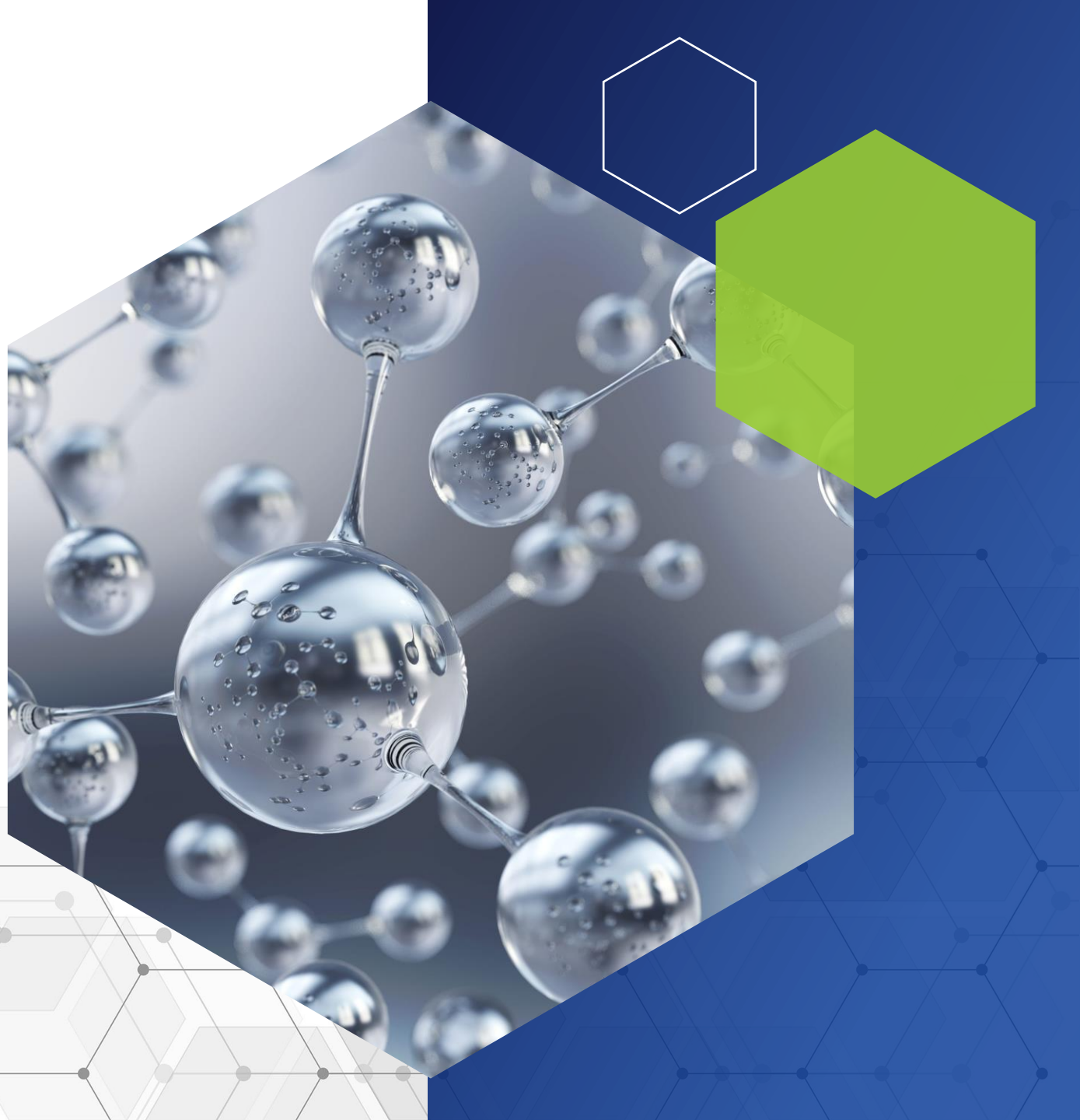




# Raymond James Human Health Innovation Conference

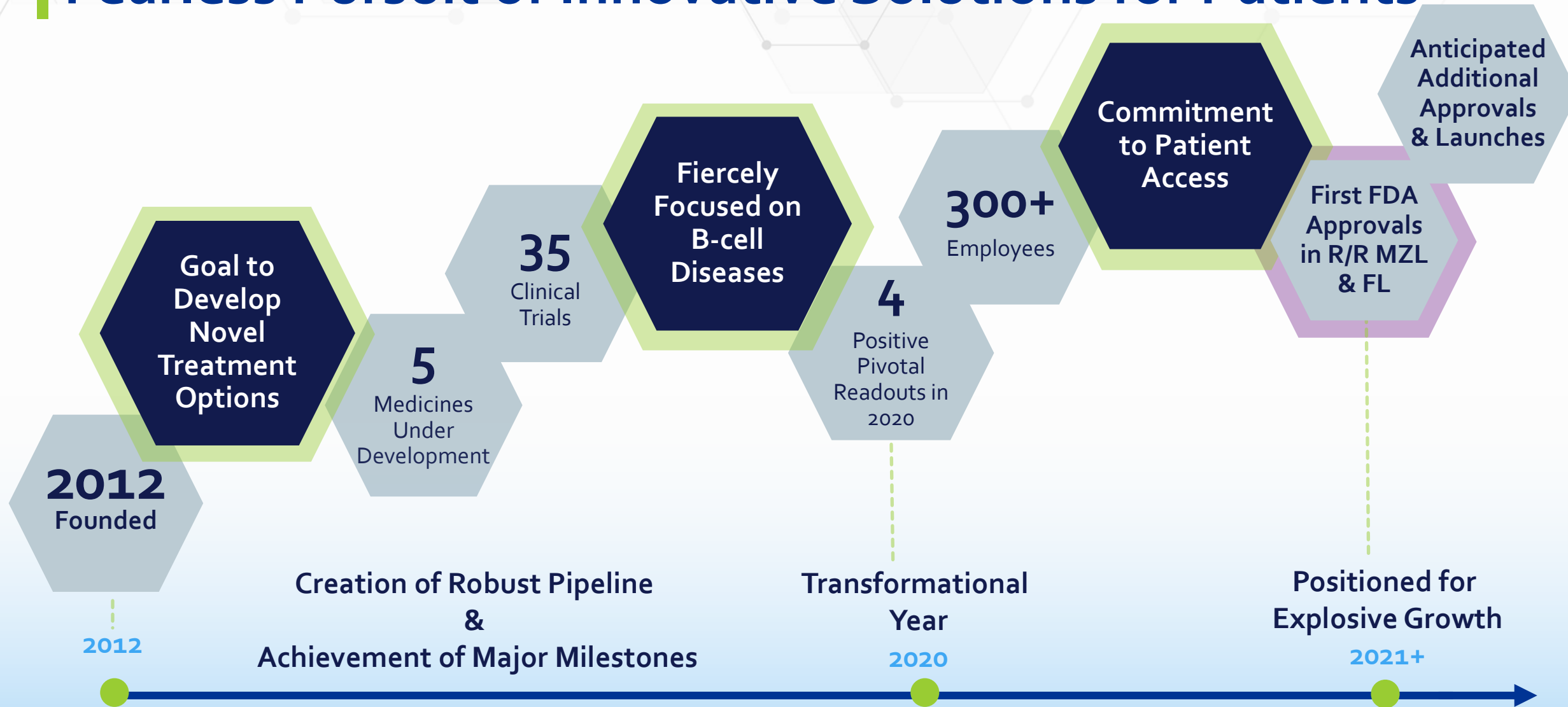
June 2021



# 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 and other risk factors identified from time to time in our reports filed with the Securities and Exchange Commission. 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.*

# Fearless Pursuit of Innovative Solutions for Patients



# Fiercely Focused on B-Cell Diseases

*Pipeline of medicines with complementary mechanisms*

MEDICINE	MECHANISM OF ACTION	STAGE OF DEVELOPMENT
UKONIQ®	PI3Kδ/CK1ε	Approved – R/R MZL and FL
Ublituximab	Anti-CD20	BLA Accepted (PDUFA 3/25/22) – U2 Positive Ph3 MS Studies
TG-1701	BTKi	Phase 1 (Monotherapy & Combo w/ U2)
TG-1801	Anti-CD47/CD19	Phase 1
Cosibelimab (TG-1501)	Anti-PD-L1	Phase 1b

# Positioned for Explosive Growth 2021+

Escalating  
Commercial  
Opportunity

## UKONIQ Monotherapy

*R/R MZL & FL*

Potential for  
Multiple FDA  
Approvals



**Differentiated  
Inhibitor of PI3K  
and CK1 $\epsilon$**

Approved for  
relapsed/refractory  
MZL & FL

## Ublituximab + UKONIQ (U2)

*Frontline & R/R CLL/SLL*

**First and Only  
Successful Ph3 of a  
PI3k in Frontline CLL**

- U2 BLA accepted
- PDUFA: 3/25/2022

## Ublituximab Monotherapy

*Relapsing MS*

**First CD20 in Ph3 to  
Achieve ARR Below  
<0.10**

- Data presented at AAN and EAN 2021
- BLA for MS target Q3 2021

## Triple Therapies

U2 + Venetoclax  
U2 + TG-1701

## Triple Combo Studies Underway

- ULTRA-V Ph2 completed enrollment
- ULTRA-V Ph3 launched!
- U2 + TG-1701 Ph1 enrolling

# UKONIQ NOW APPROVED!

*First and Only Targeted Inhibitor of PI3K-delta & CK1-epsilon*



**UKONIQ is indicated for the treatment of adult patients with:**

**MZL**

**R/R MZL who have received at least one prior anti-CD20-based regimen**

**FL**

**R/R FL who have received at least three prior lines of systemic therapy**

These indications are approved under accelerated approval based on overall response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial.



# UKONIQ Demonstrated Clinically Meaningful Benefit

*UNITY-NHL Pivotal Data in R/R MZL & FL*



✓ Durable single agent responses across R/R iNHLs

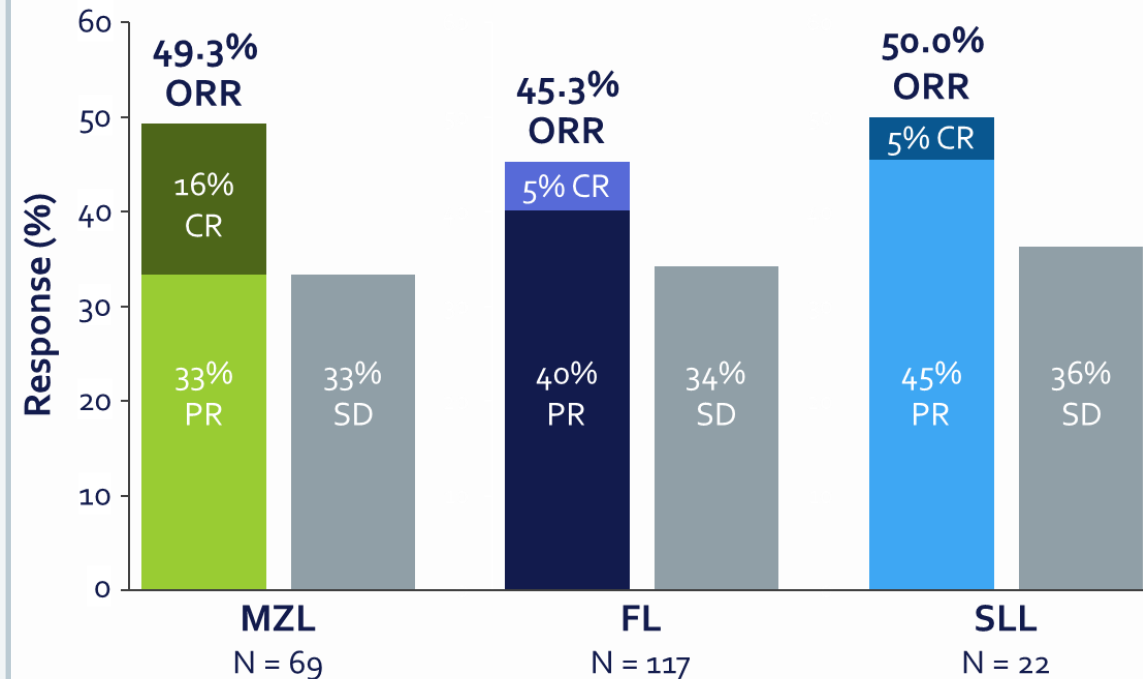
✓ No MZL Complete Responses progressed

✓ Manageable safety profile, with low incidence of immune mediated toxicities and AE related discontinuations

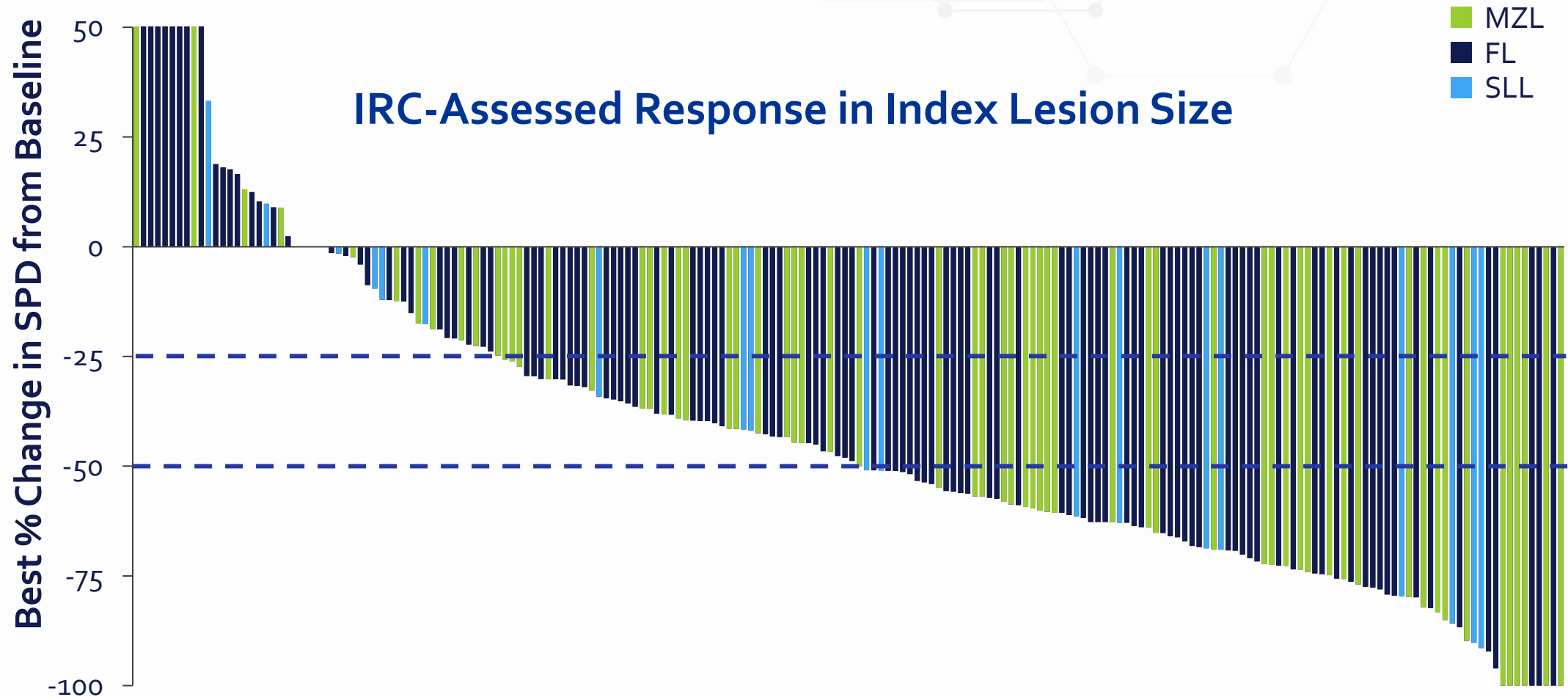
✓ UKONIQ received FDA accelerated approval

✓ R/R MZL who have received at least one prior anti-CD20-based regimen and R/R FL who have received at least three prior lines of systemic therapy

Independent Review Committee (IRC)  
Assessed Overall Response Rates (ORR)



# Most Patients Saw A Reduction in Disease Burden with UKONIQ Monotherapy



Zinzani P, et. al., ASH, December 2020



# UKONIQ Exhibited a Distinct Safety Profile

*UNITY-NHL: Extended median follow-up of 27+ months*

## LOW DISCONTINUATIONS DUE TO AEs

- 15% discontinuation rate due to AEs observed across patients with MZL, FL and SLL
- Discontinuations due to ALT/AST elevations were 2.9%
- Grade 3 diarrhea led to discontinuation of 2.9% of patients

## LIMITED GR 3/4 AEs OF SPECIAL INTEREST

- Opportunistic infections: n=7 (3.4%)
- Rash: n=4 (1.9%)
- Pneumonitis: n=2 (1.0%)
- Non-infectious colitis occurred in 4 patients (1.9%), of which 3 resolved and remained on umbralisib

*Zinzani P, et. al., ASH, December 2020*

# MZL/FL are Chronic Incurable Diseases<sup>1</sup>

*No standard of care after 1st relapse as current options are sub-optimal<sup>2</sup>*

## # of Annually Treated Patients in US<sup>3</sup>



**~8,000 to 10,000 patients estimated in potential labeled indications for UKONIQ annually<sup>3</sup>**

# Executing on Keys to UKONIQ Launch Success

Build Awareness of UKONIQ's  
Differentiated Profile



80% of target customers  
are aware of UKONIQ

Drive Adoption with Our  
Targeted Customers



Product profile  
seen as differentiated with  
engaged customers

Minimize Patient Access  
Barriers



UKONIQ is covered for  
85-90% of Medicare and  
commercial lives

**Continued execution will set the foundation for potential launch of U2 in CLL**

# Ublituximab:

*Investigational next generation anti-CD20 monoclonal antibody*

- Glycoengineered for enhanced potency
- Demonstrated activity in rituximab refractory patients<sup>1</sup>
- Shorter infusion time than approved anti-CD20's
- 2,100+ patients treated with ublituximab, including 3 randomized phase 3 trials



BLA accepted  
for U2 in  
CLL/SLL  
PDUFA: 3/25/22

Positive MS  
Ph3 Topline  
Data  
Presented at  
AAN & EAN  
2021

# Ublituximab + UKONIQ (U2) Trial Met Primary Endpoint

*UNITY-CLL Phase 3 Data*



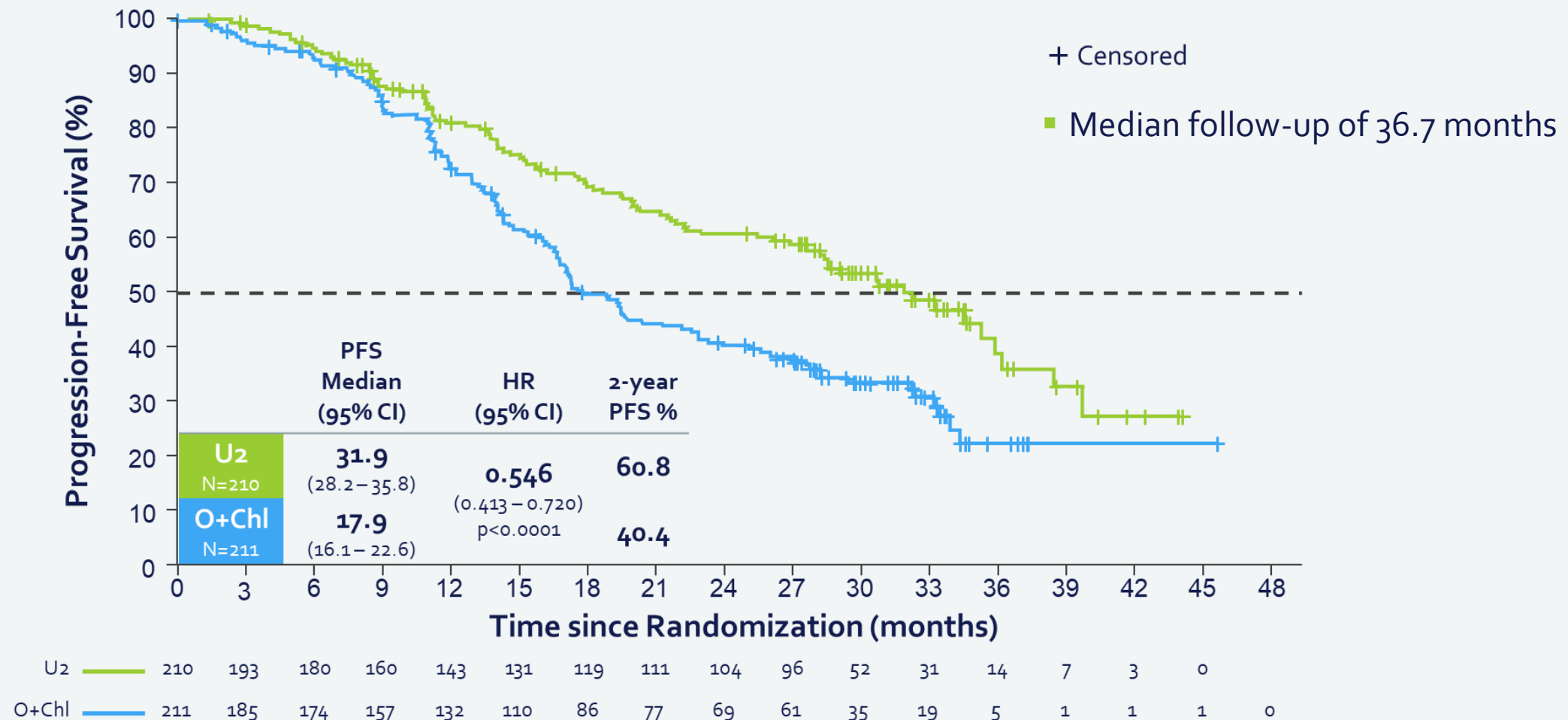
- Trial enrolled TN (57%) & R/R CLL patients and compared U2 to Obinutuzumab + Chlorambucil (O+Chl) (n=421)
- First inhibitor of PI3K to successfully treat front-line patients
- Conducted under SPA with the FDA
- U2 BLA accepted; PDUFA target goal date of March 25, 2022

Met the primary endpoint of  
**IMPROVED PROGRESSION-FREE SURVIVAL (PFS)**  
( $p < .0001$ )

Study stopped early for  
**SUPERIOR EFFICACY**  
observed at the interim analysis

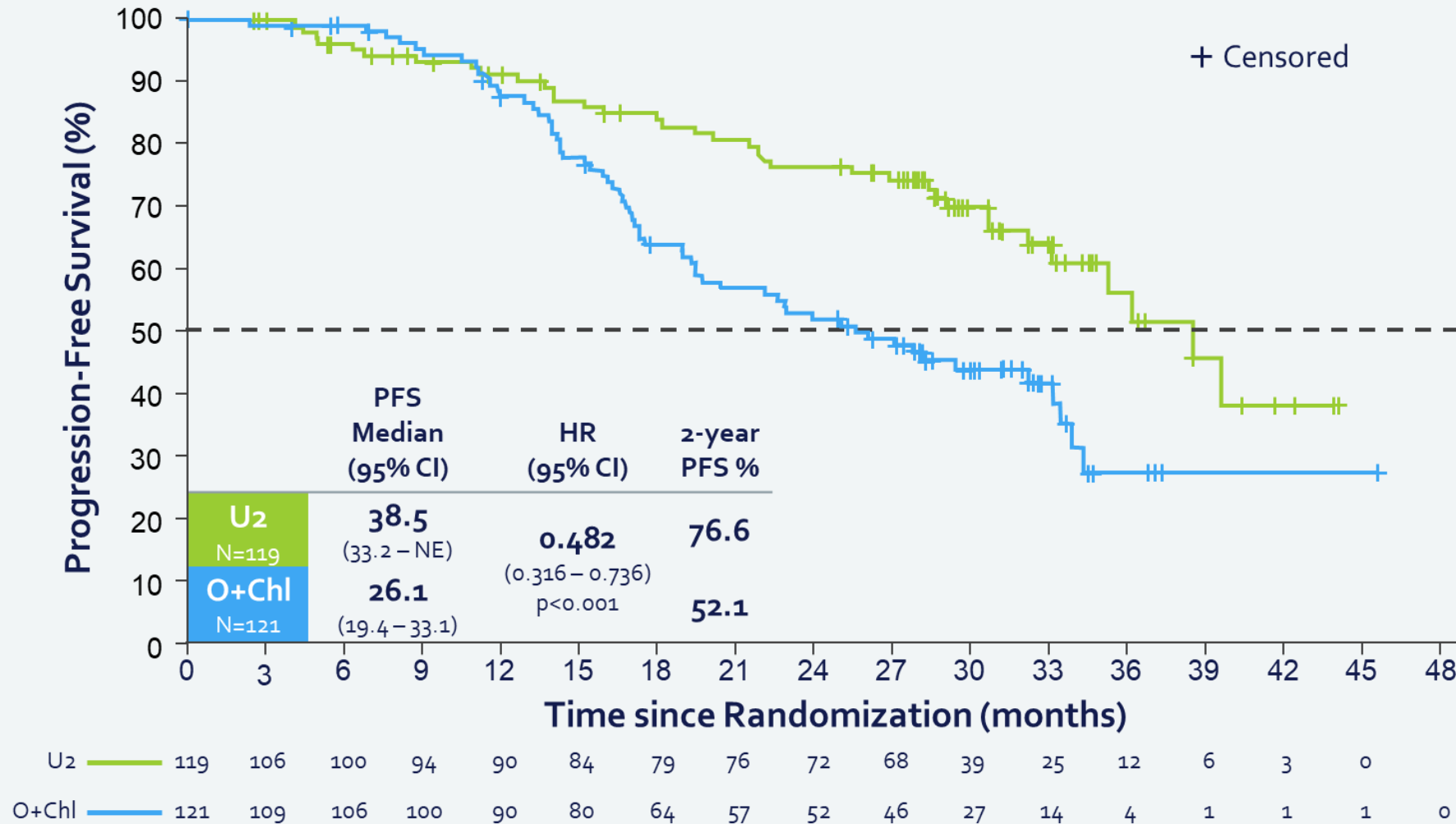
# Significantly Prolonged Progression-Free Survival

ITT Population (TN & R/R CLL)



# Significantly Prolonged Progression-Free Survival

## Treatment Naive Population





# Differentiated Safety Profile of U2 in CLL

*Safety consistent across treatment naïve and previously treated CLL*

## ALL CAUSALITY GRADE 3-4 AEs

AEs, n (%)	O + Chl <i>Treatment Naïve &amp; Previously Treated</i>	U2 <i>Treatment Naïve</i>	U2 <i>Previously Treated</i>
	N=200	N=116	N=90
Diarrhea	5 (3)	16 (13.8)	9 (10.0)
Nausea	2 (1)	1 (0.9)	2 (2.2)
Infusion related reaction	7 (4)	1 (0.9)	3 (3.3)
Fatigue	6 (3)	4 (3.4)	0
Neutropenia	70 (35)	28 (24.1)	36 (40.0)
Cough	0	0	0
Headache	1 (0.5)	0	1 (1.1)
Pyrexia	2 (1)	1 (0.9)	0
Chills	1 (0.5)	1 (0.9)	0
Upper respiratory tract infection	2 (1)	0	0
Dizziness	26 (13)	2 (1.7)	0

Gribben J, et. al, ASH 2020

# Global CLL Market Estimated to exceed \$10B by 2025<sup>1</sup>

*185,000 Americans living with CLL<sup>2</sup>; ~40,000 seeking Treatment Annually<sup>3</sup>*

## **Current Opportunity—Potential for U2 to Address Significant Unmet Need in CLL**

- **Poor Candidates for BTKi Therapy**
  - ~20% of treatment naive patients are poor candidates for BTKi therapy<sup>4</sup>
- **BTKi-Exposed Patients**
  - Large post-BTKi market with >100,000 patients previously treated<sup>5</sup>
  - ~40% discontinue BTKi due to tolerability or progression at median 17 months<sup>6</sup>

## **Future Opportunity—Potential for Addition of U2 to Standard of Care to Improve Outcomes**

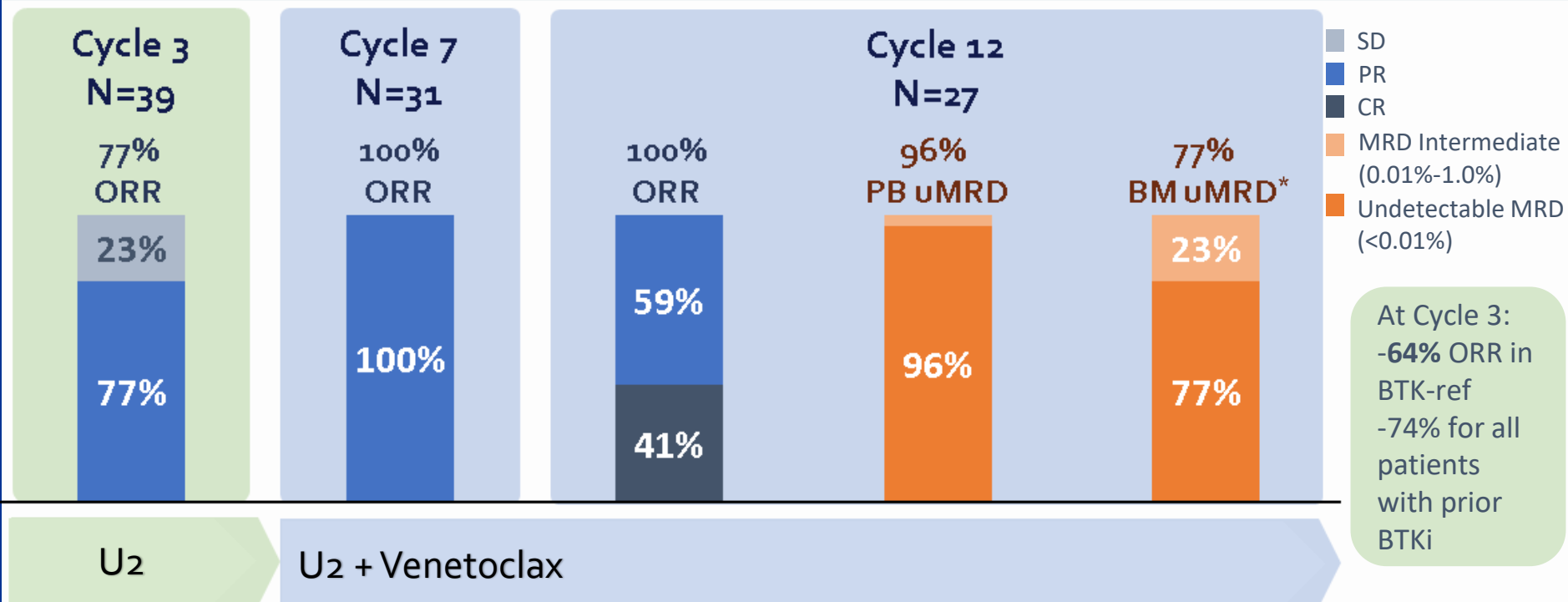
- U2 plus venetoclax and U2 plus BTKi studies underway

# U2 + Venetoclax Promising Phase 1 Early Data

*Phase 2b ULTRA-V Enrollment Complete; ULTRA-V Phase 3 Launched!*

## Phase 1 ASH 20 Data Update

 Treatment well tolerated; AEs consistent with single agent profiles



## ULTRA-V PHASE 2 ENROLLMENT COMPLETE:

- ~165 patients enrolled including patients with
  - R/R CLL
  - BTK Refractory CLL
  - Front Line CLL
- Primary Endpoint:
  - ORR & CR at 12m

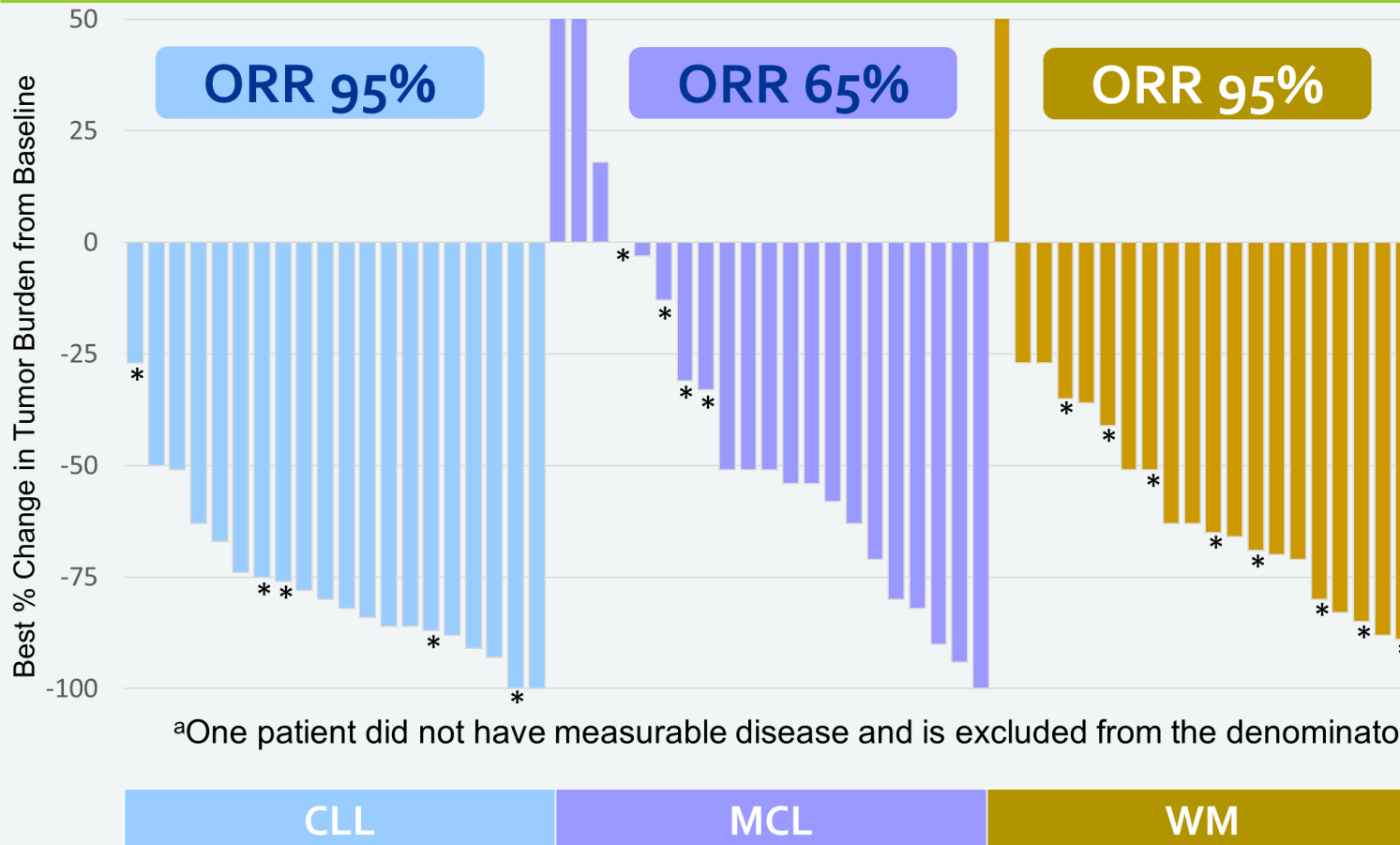
## ULTRA-V PHASE 3:

- Now enrolling patients w/:
  - R/R CLL
  - Front Line CLL
- Primary Endpoint: PFS

# TG-1701: BTKi

## Phase 1 ASCO 2021 Update

### Efficacy Disease-Specific Cohorts Monotherapy (200mg)



- N = 60
  - 20 CLL
  - 20 MCL<sup>a</sup>
  - 20 WM
- Median follow up: 12.2 mos (1.4-18.5)

\*Treatment naïve



# TG-1701: BTKi

## Phase 1 ASCO 2021 Update

### All Causality AEs (≥10%) TG-1701 Monotherapy

Adverse event, N (%)	Dose escalation (100 to 400 mg) N=25		Disease-specific cohorts (200 mg) N=61		CLL cohort (300 mg) N=20	
	Any Grade	Grade 3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Respiratory tract infection	9 (36)	2 (8)	6 (10)	-	2 (10)	-
Constipation	8 (32)	-	3 (5)	-	-	-
Bruising	7 (28)	-	5 (8)	-	-	-
Fatigue	5 (20)	-	2 (3)	-	1 (5)	-
Rash	4 (20)	1 (4)	3 (5)	-	1 (5)	-
Nausea	4 (16)	-	1 (2)	-	2 (10)	-
Dizziness	4 (16)	-	1 (2)	-	-	-
Headache	3 (12)	-	6 (10)	-	1 (5)	-
Diarrhea	3 (12)	-	7 (11)	-	2 (10)	-
Epistaxis	3 (12)	-	2 (3)	-	-	-
COVID-19	-	-	4 (7)	1 (2)	3 (15)	2 (10)
<b>Hematologic and lab abnormalities</b>	<b>Any Grade</b>	<b>Grade 3</b>	<b>Any Grade</b>	<b>Grade ≥3</b>	<b>Any Grade</b>	<b>Grade ≥3</b>
Neutropenia	6 (24)	2 (8)	8 (13)	5 (8)	2 (10)	2 (10)
ALT increased	6 (24)	3 (12) <sup>a</sup>	5 (8)	1 (2)	3 (15)	1 (5)
AST increased	5 (20)	1 (4)	3 (5)	-	3 (15)	1 (5)
Anemia	4 (16)	-	7 (11)	3 (5)	-	-

- There have been no G<sub>4</sub> AEs in the dose escalation of monotherapy
- At 200mg and 300 mg QD (n=81), AE's of special interest were G<sub>3</sub> hypertension 4.9% and atrial fibrillation 1.2%. There have been no instances of major bleeding

<sup>a</sup>All at 400 mg QD. 2 cases were brief episodes in asymptomatic pts with normal liver function (total bilirubin within normal range).  
1 case was in the context of significant progression of disease in the liver.

# Ublituximab in RMS Demonstrated Unprecedented ARR

*<0.10 ARR in each of the ULTIMATE I & II Phase 3 studies*



- 1,094 RMS patients enrolled across 10 countries randomized 1:1 to ublituximab or teriflunomide
- Trials conducted under SPA with the FDA
- Full data presented at AAN and EAN 2021
- BLA submission target Q3 2021

## ULTIMATE I & II Phase 3 Results

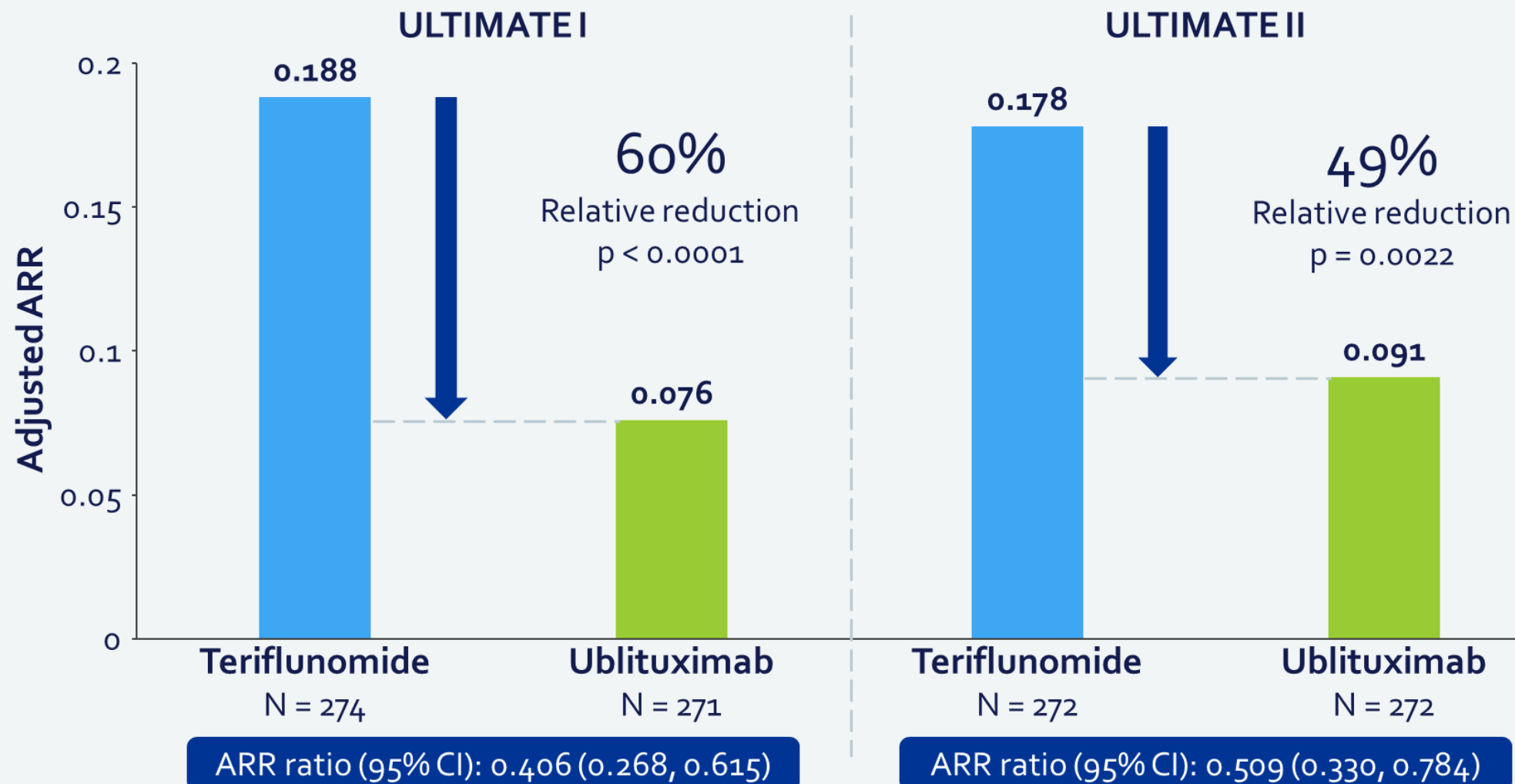
**<0.10 ARR**

Lowest reported in a Phase 3

**Ublituximab was generally well-tolerated with no unexpected safety signals**



# ULTIMATE I & II Phase 3 Data of Ublituximab in RMS

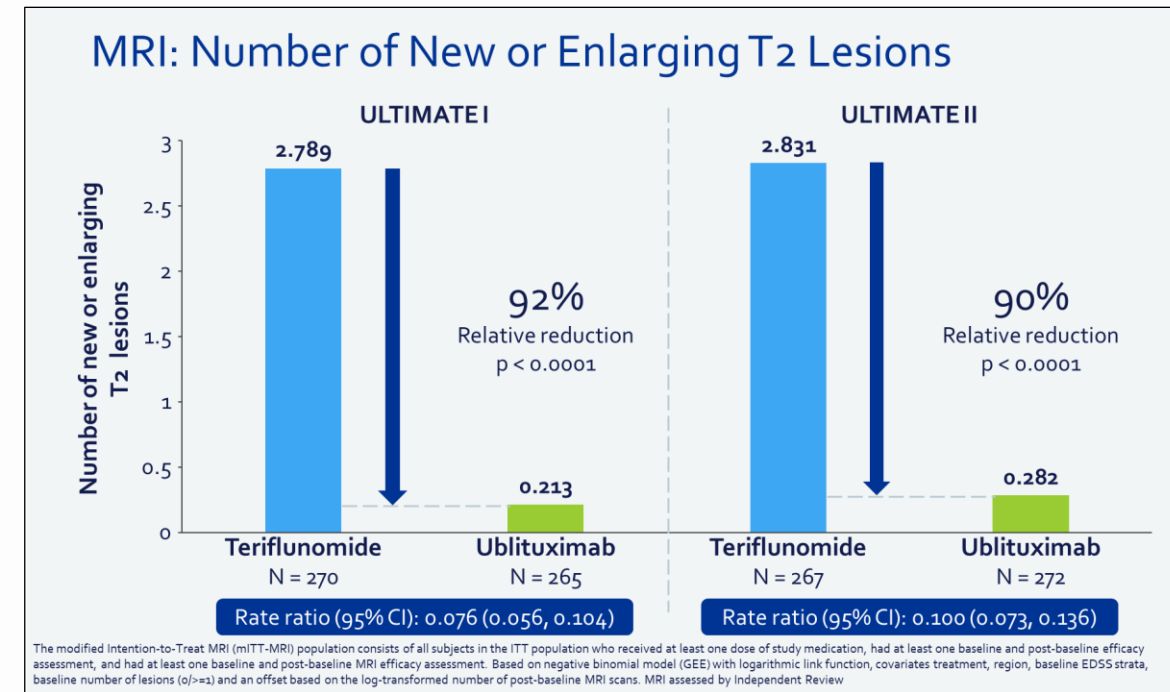
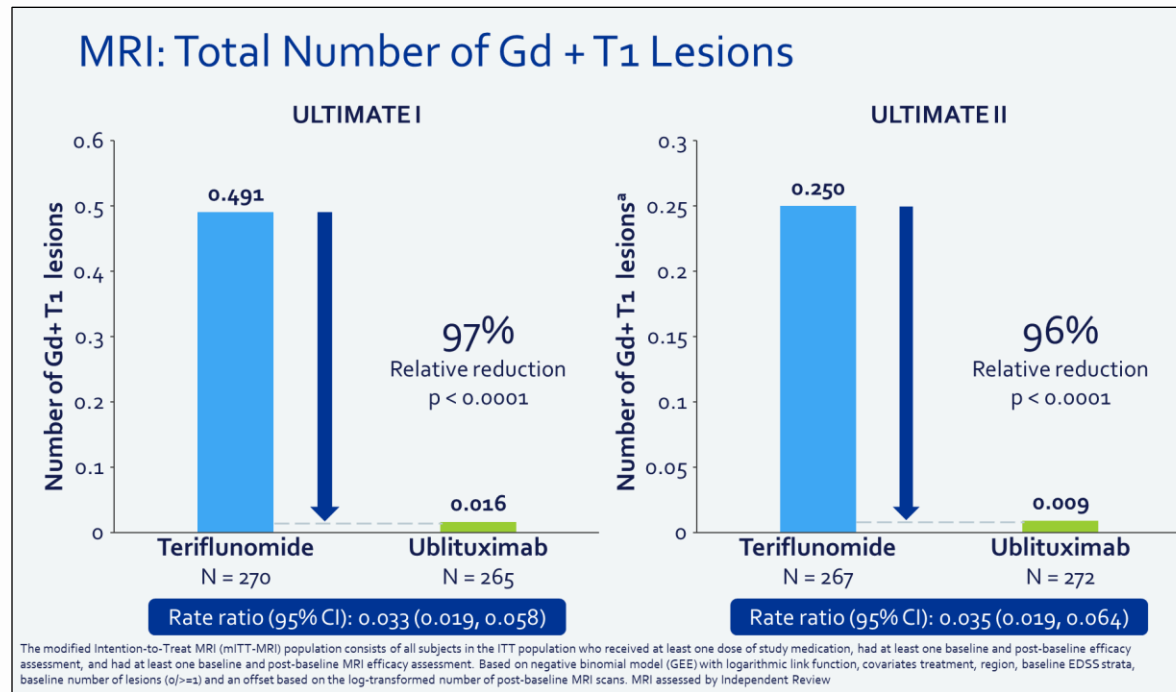


The modified Intention-to-Treat (mITT) population consists of all subjects in the ITT population who received at least one dose of study medication and had at least one baseline and post-baseline efficacy assessment. Based on negative binomial model (GEE) for the relapse count per subject with logarithmic link function, treatment, region, and baseline EDSS strata as covariates and log (years of treatment) as offset. CI: confidence interval.

# ULTIMATE I & II Phase 3 Data of Ublituximab in RMS

## Secondary Endpoints

- 97% and 96% relative reduction in T1 Gd enhancing lesions ( $p < 0.0001$ )
- 92% and 90% relative reduction in new or enlarging T2 lesions ( $p < 0.0001$ )

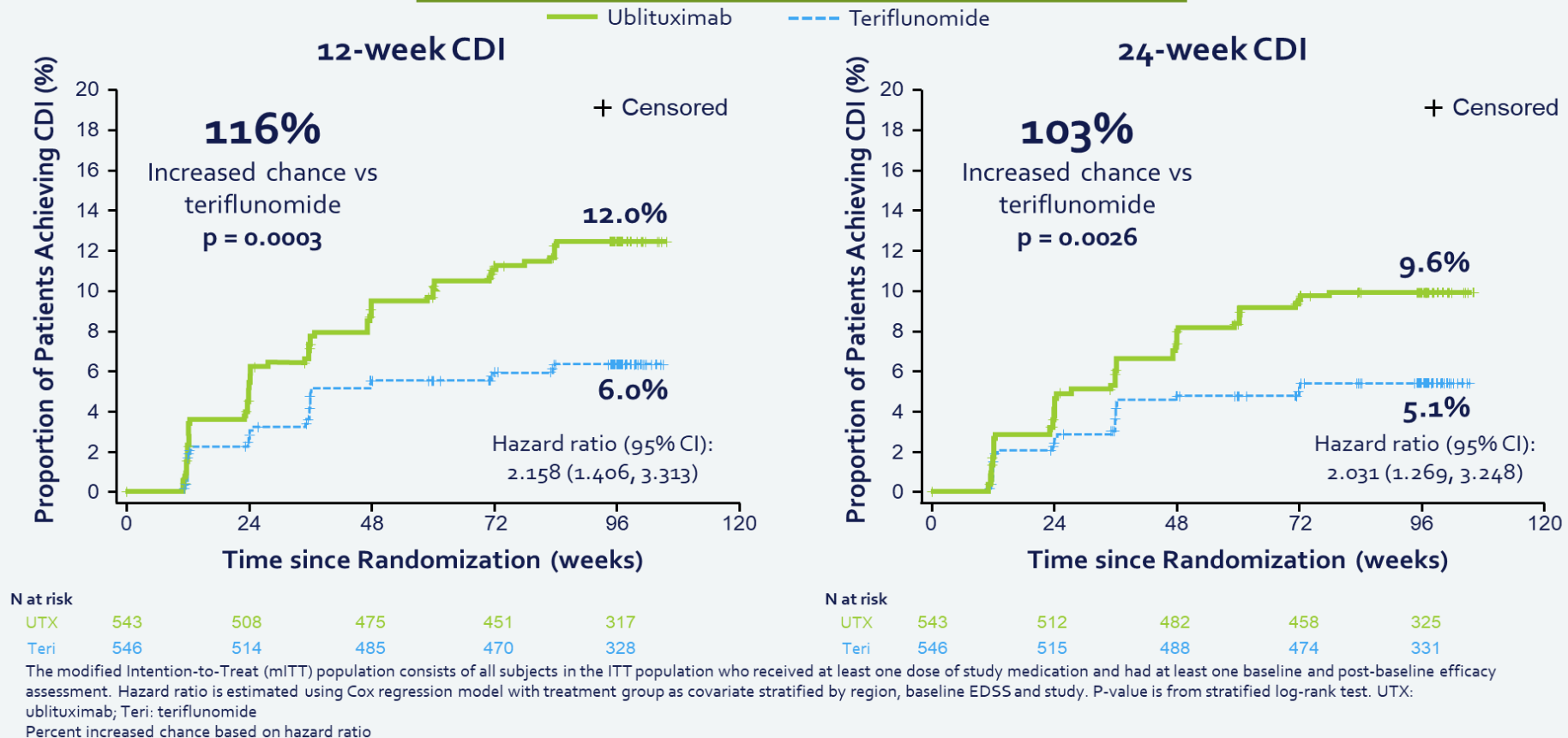


# ULTIMATE I & II Phase 3 Data of Ublituximab in RMS

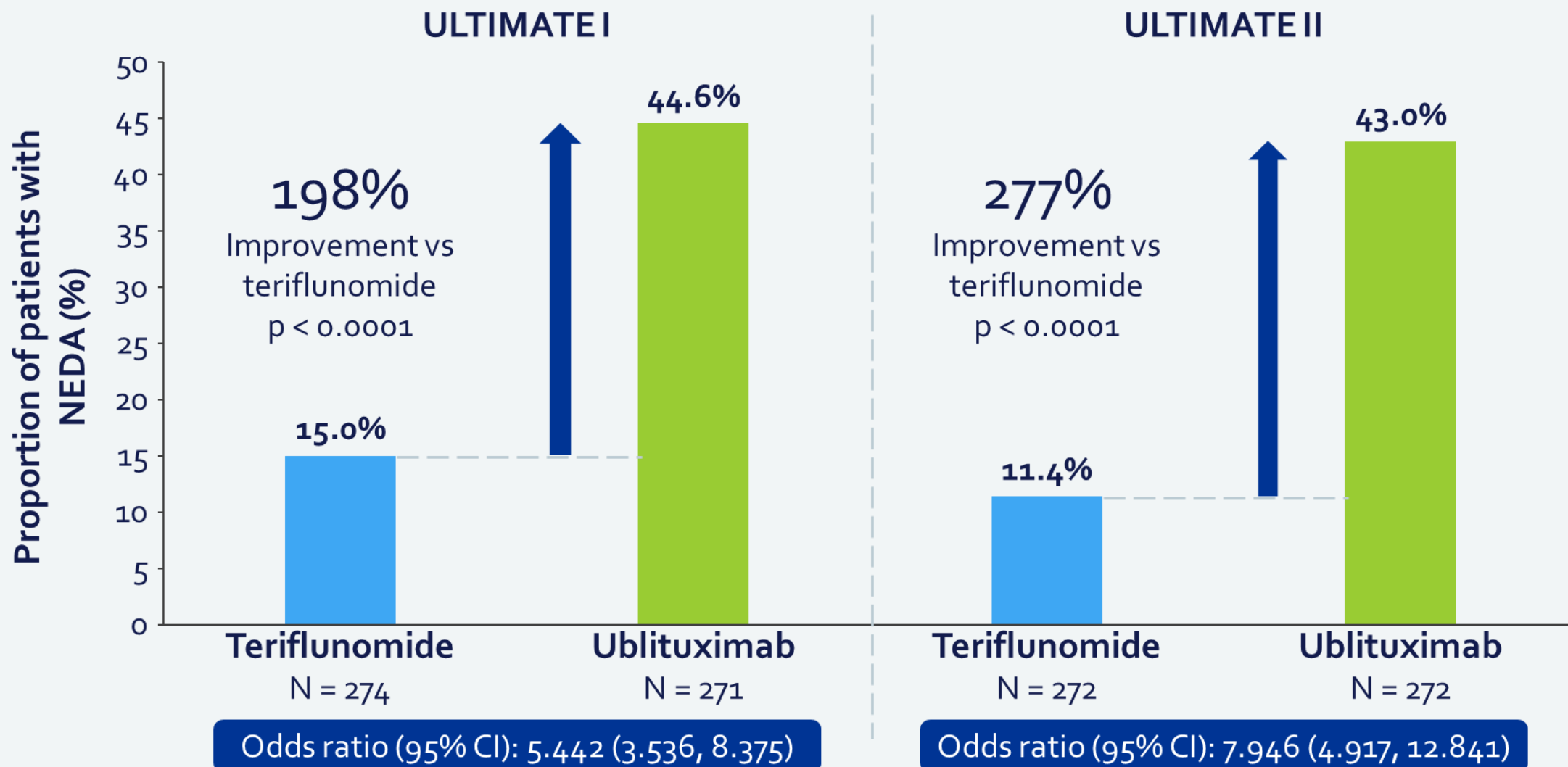
A very low rate of disability progression was observed across all treatment groups

- 5.2% for ubli v. 5.9% teri for 12-week confirmed disability progression (CDP)
- 3.3% for ubli v. 4.8% teri showed 24-week CDP
- There was no statistically significant difference in CDP between treatment arms

## Confirmed Disability Improvement (CDI)



# ULTIMATE I & II Phase 3 Data of Ublituximab in RMS



The modified Intention-to-Treat (mITT) population consists of all subjects in the ITT population who received at least one dose of study medication and had at least one baseline and post-baseline efficacy assessment. Logistic regression model with covariates treatment, region, baseline EDSS strata and log transformed baseline MRI counts (T1 unenhancing, T2, Gd enhancing).

# ULTIMATE I & II: Adverse Events

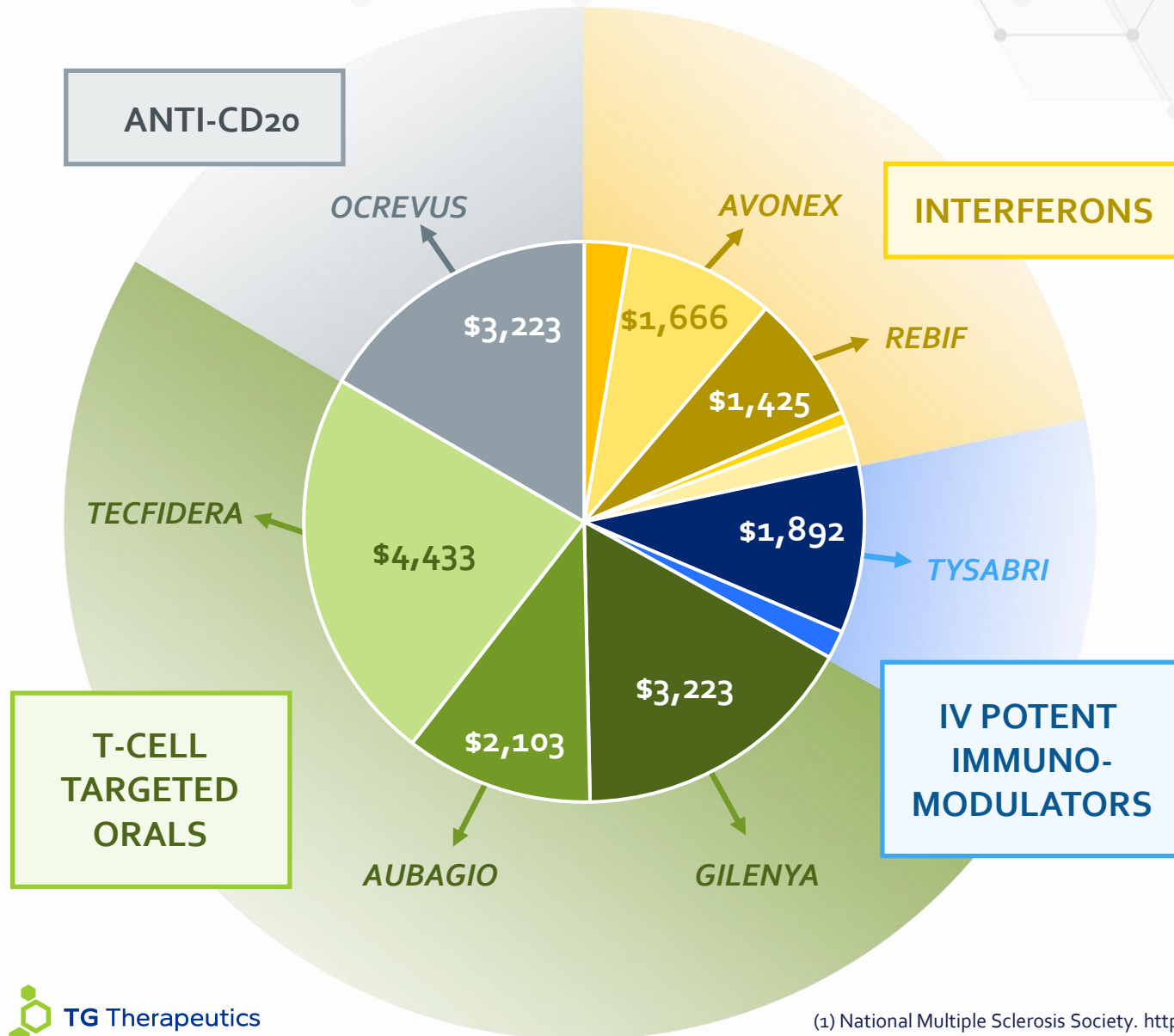
Most common AEs, n (%) ≥5% in any treatment group	Teriflunomide N=548	Ublituximab N=545
Any AE	486 (88.7)	483 (88.6)
IRR	67 (12.2)	260 (47.7)
Headache	138 (25.2)	165 (30.3)
Nasopharyngitis	96 (17.5)	97 (17.8)
Lymphopenia	5 (0.9)	51 (9.4)
Back pain	53 (9.7)	48 (8.8)
Respiratory tract infection viral	31 (5.7)	41 (7.5)
Respiratory tract infection	38 (6.9)	40 (7.3)
Upper respiratory tract infection	33 (6.0)	39 (7.2)
Diarrhea	53 (9.7)	36 (6.6)
Lymphocyte count decreased	9 (1.6)	34 (6.2)
Abdominal pain	17 (3.1)	32 (5.9)
Pharyngitis	11 (2.0)	31 (5.7)
Pyrexia	23 (4.2)	30 (5.5)
Insomnia	16 (2.9)	28 (5.1)
Nausea	26 (4.7)	28 (5.1)
Hypertension	35 (6.4)	19 (3.5)
Alopecia	84 (15.3)	18 (3.3)

# ULTIMATE I & II: Serious Adverse Events

SAEs, n (%)	Teriflunomide N = 548	Ublituximab N = 545
Any serious AEs	34 (6.2)	52 (9.5)
<b>Most common SAEs by SOC</b> <i>≥1% in any treatment group</i>		
Infections and infestations	14 (2.6)	22 (4.0)
Nervous system disorders	7 (1.3)	5 (0.9)

- Three total malignancies were reported
  - 2 ublituximab (endometrial, uterine) versus teriflunomide 1 (tongue)
- Three total deaths occurred
  - Ublituximab: pneumonia, encephalitis (post-measles), salpingitis
  - 1 death was deemed possibly related to treatment (pneumonia)
- No cases of progressive multifocal leukoencephalopathy (PML)

# Significant Market Opportunity For Ublituximab in MS



~1M Patients Living with MS in the U.S.<sup>1</sup>

Rapidly growing market: \$20B U.S. market growing to \$28B by 2025<sup>2</sup>

Anti-CD20 utilization in MS expanding steadily and expected to grow to >\$10+B by 2025<sup>3</sup>

Multiple \$1B+ Treatment Options Coexist in U.S. Market

~5,000 Physicians Treat ~80% of the patients



# Ublituximab Offers Potentially Best-In Class Profile

## Ublituximab for RMS

### CLINICAL



Only anti-CD20 to demonstrate  
ARR <0.10 in Phase 3

### CONVENIENCE



1 hour infusion  
every 6 months  
(after 1<sup>st</sup> infusion)










### ACCESS



Plan to  
strategically price to  
optimize patient access

# Positioned to Achieve Multiple Projected Milestones in 2021

*~\$524m cash as of Q1 2021*

REGULATORY	COMMERCIAL	CLINICAL & PIPELINE
 UKONIQ Approved in R/R MZL and R/R FL	 Execute successful UKONIQ launch for R/R MZL and FL	 Completion of ULTRA-V Ph2B enrollment
 Acceptance of U2 CLL/SLL BLA– 3/25/22 PDUFA	 Prepare for CLL and MS launches	 ULTIMATE I&II full data – 1H
 Ublituximab MS BLA submission – Q3 2021		 Additional triplet data
		 Advance early-stage pipeline





# TG Therapeutics

**NASDAQ: TGTX**