



# TG Therapeutics

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October 2019

# 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 is a biotechnology company focused on developing medicines for patients with B- cell diseases:***

## ***Cancer***

- **Chronic Lymphocytic Leukemia**
- **Marginal Zone Lymphoma**
- Follicular Lymphoma
- Diffuse Large B-Cell Lymphoma

## ***Autoimmune***

- **Multiple Sclerosis**
- Myasthenia Gravis
- Rheumatoid Arthritis
- Lupus

# Unique Approach to Drug Development

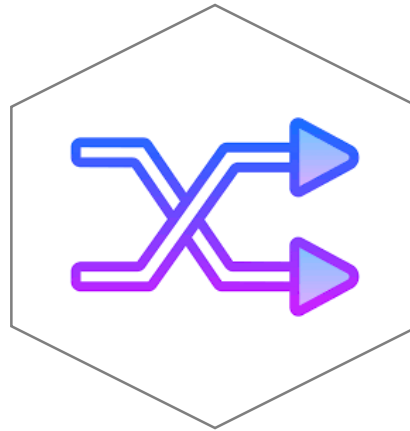
## IDENTIFY



**Identify validated targets for B-cell diseases**

- Based on preclinical or clinical data known to be important in the treatment of B-cell disease

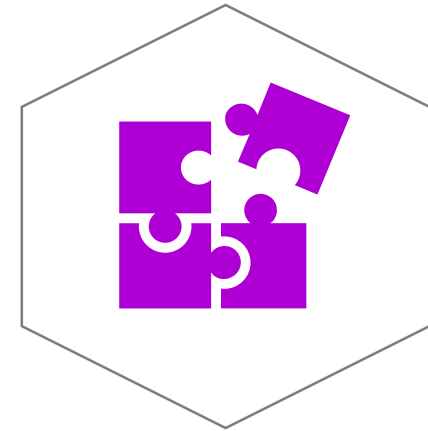
## ACQUIRE



**Search & Acquire "Best-in-Class" Compounds**

- Compounds that have the potential to offer improvements over available therapies

## DEVELOP



**Develop Multi-drug Combinations**

- To develop functional cures for cancers requires multiple drugs...*solutions development*

# B-Cell Focused Platform

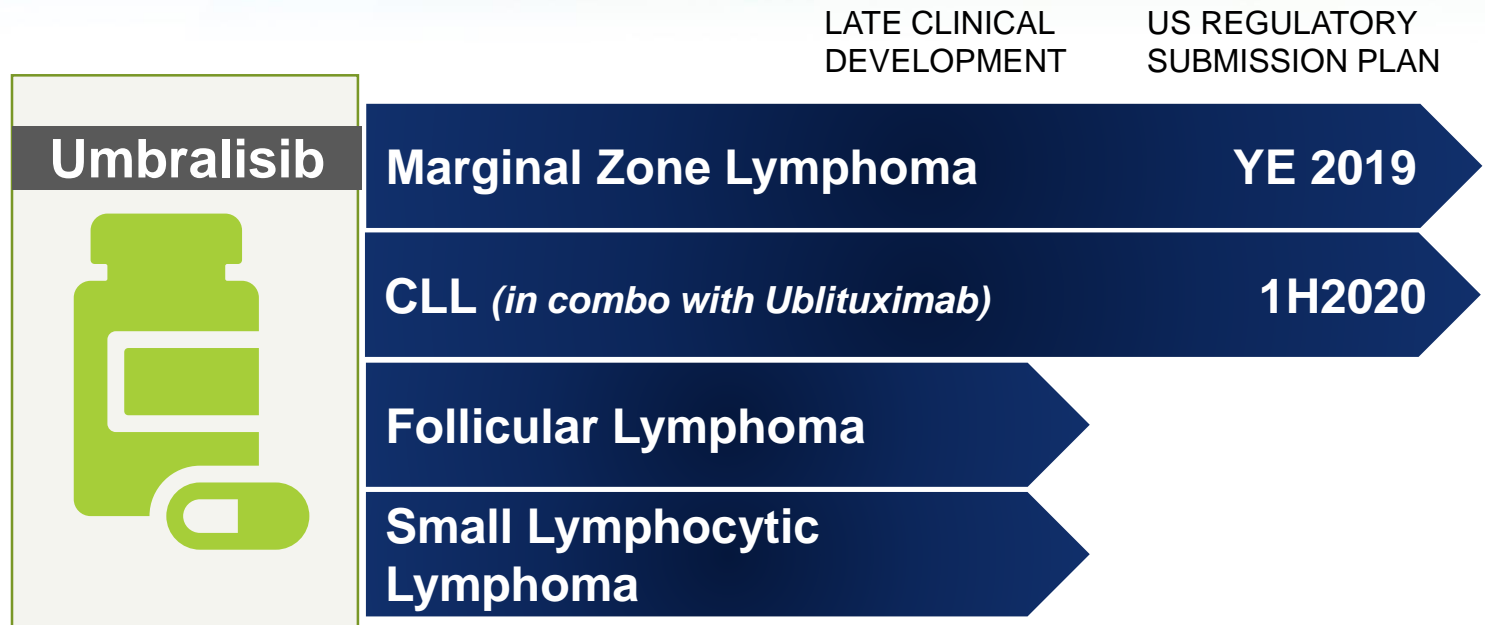
## Clinical Stage Portfolio Overview

Product	Mechanism of Action	Stage of Development
<b>Umbralisib</b> <i>(TGR-1202)</i>	PI3K $\delta$ /CK1 $\epsilon$	Phase 3
<b>Ublituximab</b> <i>(TG-1101)</i>	Anti-CD20	Phase 3
<b>TG-1501</b>	Anti-PD-L1	Phase 1b
<b>TG-1701</b>	BTKi	Phase 1
<b>TG-1801</b>	Anti-CD47/CD19	Phase 1



# Umbralisib:

## Investigational Targeted Therapy with “Best-in-Class” Potential



### Next Generation PI3K delta inhibitor

Overcomes 1<sup>st</sup> generation Toxicity

Activity across NHL and CLL

Once daily oral dosing vs. BID or IV

# First Generation PI3K-delta's are highly active but tolerability has limited market utilization

## Idelalisib

### Black-Box Warning<sup>(1)</sup>

- **Fatal and/or serious hepatotoxicity occurred in 16% - 18%** of Zydelig-treated patients
- **Fatal and/or serious diarrhea or colitis occurred in 14% - 20%** of Zydelig-treated patients
- **Fatal and/or serious pneumonitis occurred in 4%** of Zydelig-treated patients
- **Fatal and/or serious infections occurred in 21% - 48%** of patients treated with Zydelig monotherapy

## Duvelisib

### Black-Box Warning<sup>(2)</sup>

- **Fatal and/or serious infections occurred in 31%** of Copiktra-treated patients
- **Fatal and/or serious diarrhea or colitis occurred in 18%** of Copiktra-treated patients
- **Fatal and/or serious cutaneous reactions occurred in 5%** of Copiktra-treated patients
- **Fatal and/or serious pneumonitis occurred in 5%** of Copiktra-treated patients

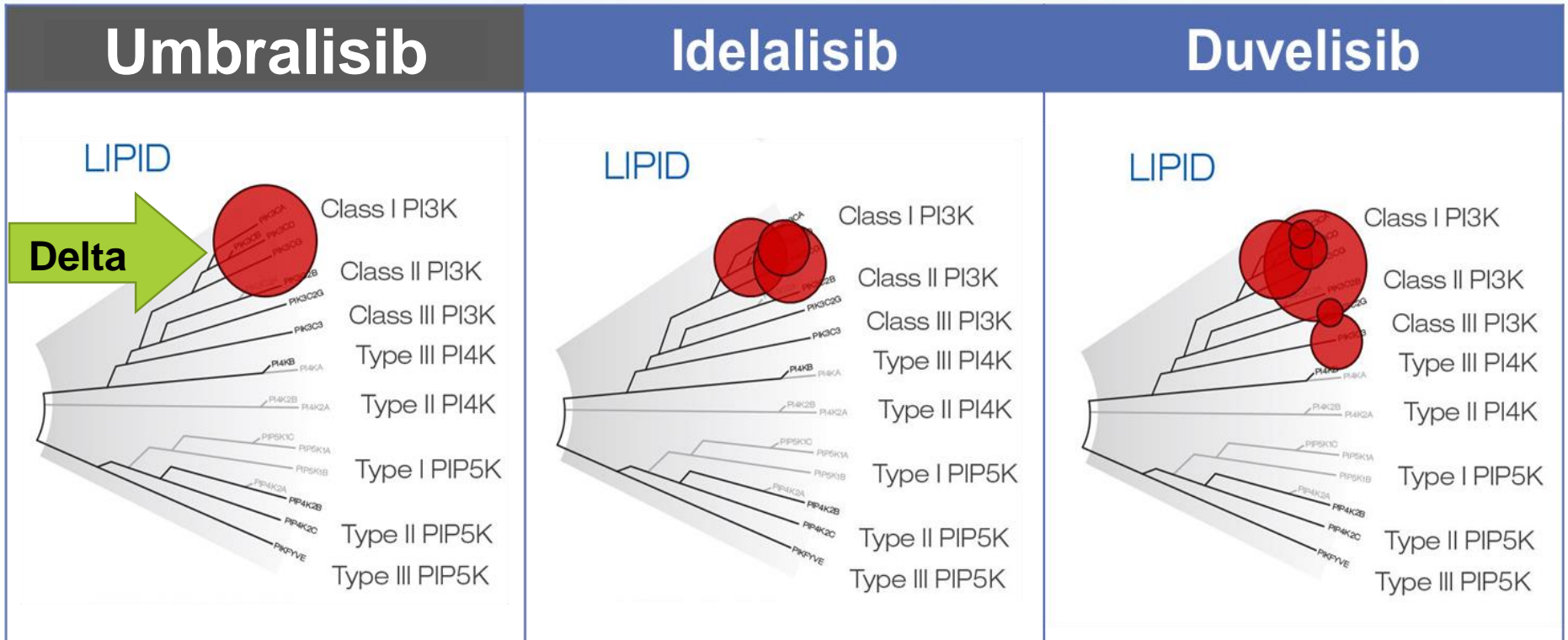
## Copanlisib

### Warnings and Precautions<sup>(3)</sup>

- **Infections: Serious, including fatal, infections occurred in 19%** of Aliqopa-treated patients
- **Hyperglycemia: Grade 3 or 4 hyperglycemia occurred in 41%** of Aliqopa-treated patients
- **Hypertension: Grade 3 hypertension occurred in 26%** of Aliqopa-treated patients
- **Non-Infection Pneumonitis: Occurred in 5%** of Aliqopa-treated patients
- **Severe Cutaneous Reactions: Grade 3 and 4 cutaneous reactions occurred in 2.8% and 0.6%** of Aliqopa-treated patients, respectively

➤ **Market is in need of a well tolerated PI3K-delta**

# Umbralisib: Selectivity



*In-vitro kinase profiling – all compounds at 1µM*

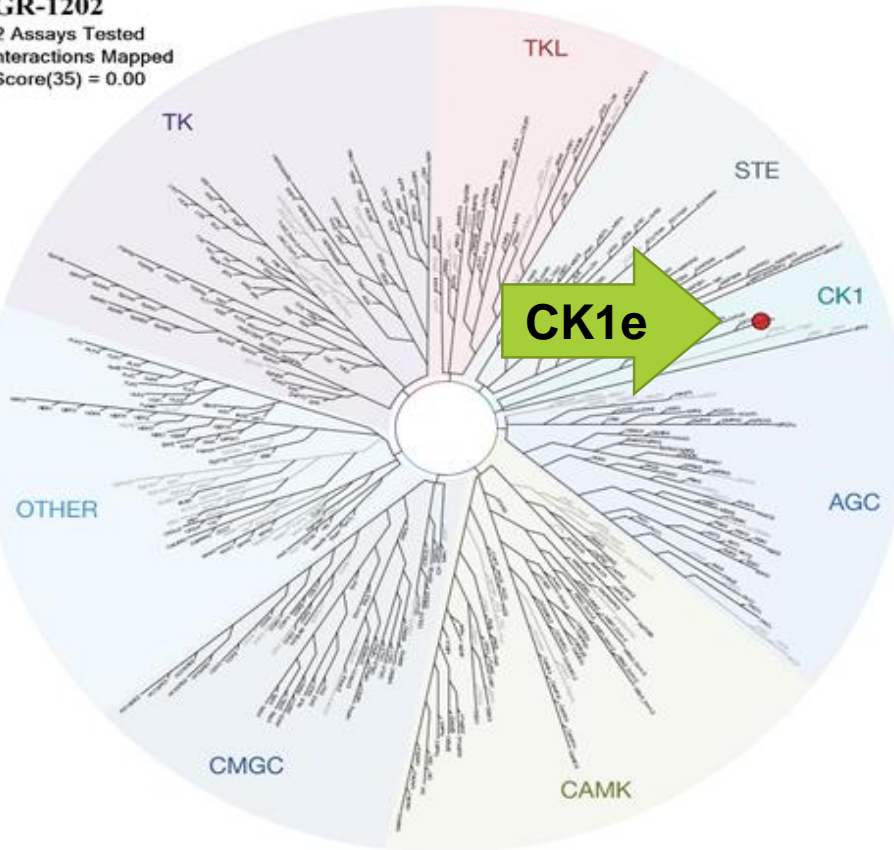
- **Umbralisib exhibits greater selectivity to PI3k-delta compared to other PI3K inhibitors**
- Red circles indicate which kinase is being inhibited
- The larger the red circle, the stronger the relative inhibition of the kinase



# Umbralisib: Selectivity

## Umbralisib

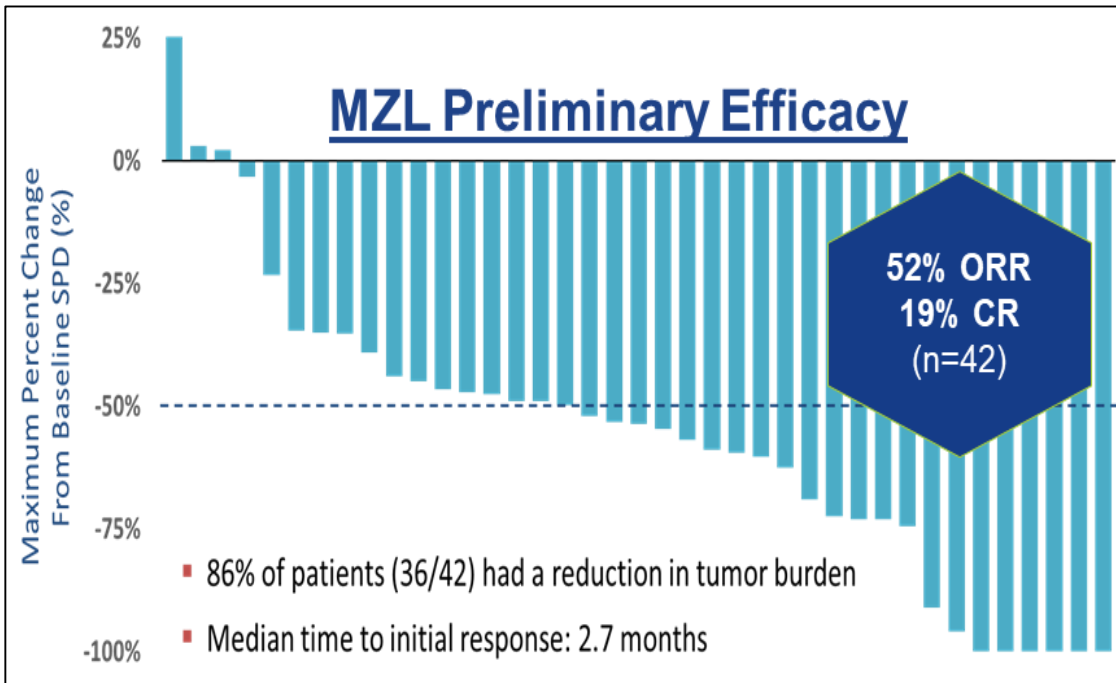
TGR-1202  
442 Assays Tested  
3 Interactions Mapped  
S-Score(35) = 0.00



- PI3K associated immune-mediated toxicities are thought to be related to impaired Tregs (Lampson et al., Blood 2016)
- Umbralisib uniquely inhibits CK1-epsilon, an important conduit which may play a role in Treg development and function
- Combination of CK1-epsilon targeting and lack of inhibition of PI3K gamma may prevent impairment of Tregs, explaining the improved tolerability profile observed for umbralisib.

# Data Supporting Planned Umbralisib Filing In MZL *Breakthrough Therapy Designation Granted*

- MZL Trial met primary endpoint exceeding target 40% ORR
- ***Following Discussions with FDA Plan to Commence Rolling Submission around YE2019***



## **MZL Preliminary Safety & Tolerability**

- Umbralisib was deemed to be well tolerated
- No events of colitis reported
- AE's leading to dose reduction occurred in 6 subjects (9%)
- 10 subjects (14%) discontinued umbralisib due to an AE considered at least possibly related to treatment
- No deaths occurred on study
- Grade 3 infections were limited, occurring in 3 patients (bronchitis, pneumonia, and influenza)

# MZL patients have few treatment options and no available cures

- Approximately 7,500 new cases per year, with ~3,000 relapsed patients needing treatment each year
- Second largest indolent form of NHL
- Affects mostly elderly individuals



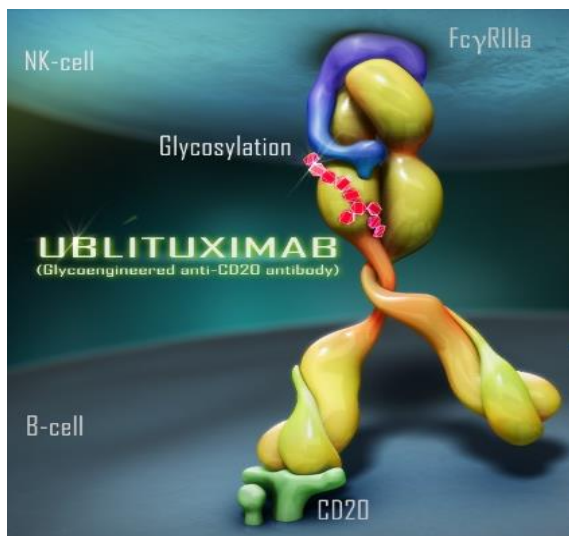
- **Chemo-immunotherapy:** non-specific, toxic contraindicated in certain unfit elderly patients
- **R<sup>2</sup>:** recently approved Revlimid plus Rituxan– can cause severe neutropenia and rash; secondary malignancy risks
- **Ibrutinib:** accelerated approval – less than half of patients respond; tolerability issues
- **PI3K Delta inhibitors:** none approved

- Need for highly active, well-tolerated treatment option for MZL

**Umbralisib: Convenient oral daily dosing appears well tolerated with ~50% ORR in MZL**

# Ublituximab:

## *Investigational Next Generation Anti-CD20 Monoclonal Antibody*



LATE CLINICAL  
DEVELOPMENT

US REGULATORY  
SUBMISSION PLAN

**CLL (*in combo with umbralisib*)**

**1H 2020**

**Multiple Sclerosis**

**YE 2020**

### Ublituximab

Glycoengineered for enhanced potency over 1<sup>st</sup> generation

Activity in Rituxan refractory patients

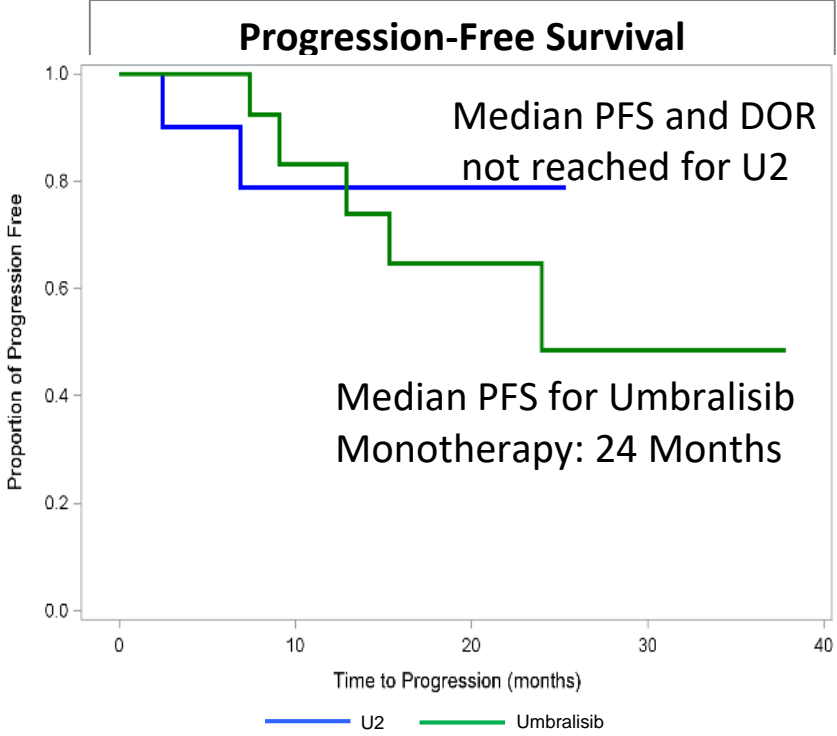
Shorter infusions than all other anti-CD20s (1-1.5 v 3-4 hours)

# Early Clinical Data for Umbralisib and U2 in CLL Support Successful Phase 3

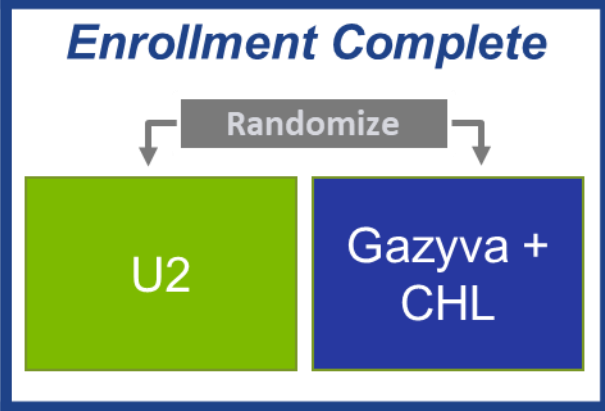


**85% ORR**  
*Umbralisib monotherapy (at higher doses)*

*(Published in Lancet Oncology February 2018)*



## UNITY-CLL



Study Enrollment	~420
Primary Endpoint	PFS
Target PFS Readout	2H-19/1H-20
Patient Population	1L/2L+

**Conducted under Special Protocol Assessment**

Mato A, et. al, EHA 2016

# CLL is One of the Fastest Growing Global Hematology Markets

- ~115,000 Americans living with CLL
- ~20,000 newly-diagnosed patients each year
- ~20,000 previously treated patients seeking treatment each year



# CLL remains incurable despite new treatment options

- **Chemo-immunotherapy:** non-specific, toxic contraindicated in certain unfit elderly patients
- **BTK inhibitors:** tolerability issues can be significant
- **PI3K delta inhibitors:** tolerability prevents widespread utilization; idelalisib contraindicated in first line therapy
- **BCL2 inhibitors:** potential for severe tumor lysis syndrome requires enhanced monitoring and hospitalization in many cases



- 50,000+ patients treated in the US
- 135,000 patients treated WW

➤ ***Need for additional highly active, well-tolerated treatments for CLL***



# U2 Offers a Needed Novel Treatment Option for CLL

## Alternative to or Complementary with Standard of Care

	Community-based Practices (~85%* of Care) <sup>1</sup>	Academic-based Practices (~15% of Care) <sup>1</sup>
BTK Naïve Patients	<ul style="list-style-type: none"> <li>▪ <b>U2</b> (in poor candidates for BTK)</li> <li>▪ <b>U2+BTK</b> (to enhance efficacy)</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>U2</b> (in poor candidates for BTK/Ven)</li> <li>▪ <b>U2+BTK</b> (to enhance efficacy)</li> <li>▪ <b>U2+Venetoclax</b> (curative intent)</li> </ul>
BTK Treated Patients	<ul style="list-style-type: none"> <li>▪ <b>U2</b> (in patients rel/ref/intolerant to BTK)</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>U2</b></li> <li>▪ <b>U2+Venetoclax</b> (curative intent)</li> </ul>

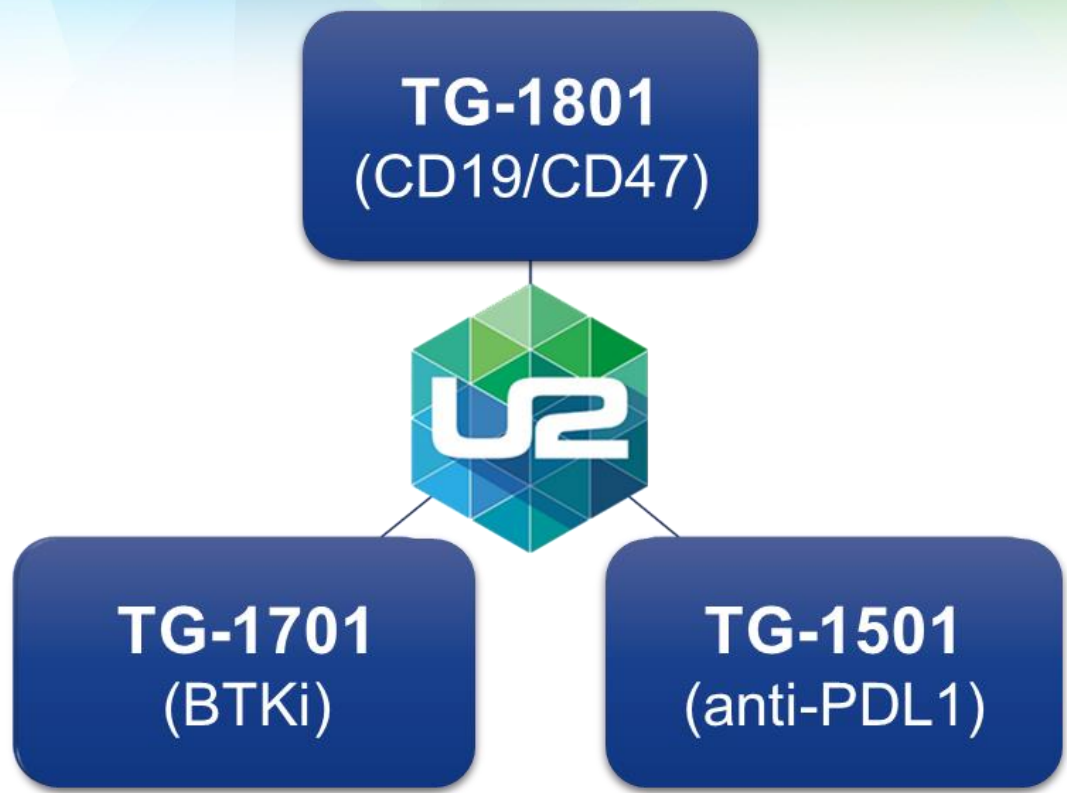
\*Venetoclax currently has limited utilization in the community due to monitoring/safety challenges

<sup>1</sup>Oncology Nursing Society, 2016

This slide represents the landscape from the Company's perspective. Actual results may differ materially from those assumed by the Company and should not be relied upon for any purpose.



# B-Cell Platform Provides Next Gen Combo's



## Ublituximab + Umbralisib (U2) + Ibrutinib

Response Rate Observed with Triple Therapy

Type	Pts (n)	CR <sup>+</sup> (n)	PR (n)	ORR n (%)
CLL/SLL	19	6	13	19 (100%)
MZL	2	1	1	2 (100%)
MCL	4	2	2	4 (100%)
FL	5	1	3	4 (80%)
DLBCL	6	-	1	1 (17%)
<b>Total</b>	<b>36</b>	<b>10</b>	<b>20</b>	<b>30 (83%)</b>

Nastoupil et al, Lugano 2017

## Ublituximab + Umbralisib + Pembro

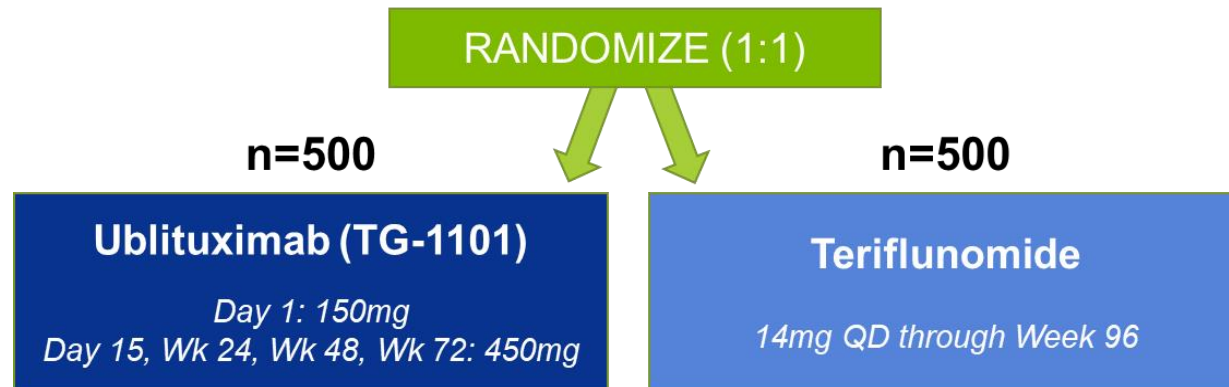
Response Rate Observed with Triple Therapy

Group	N	CR N (%)	PR N (%)	ORR N (%)
CLL	10	1 (10%)	8 (80%)	<b>9 (90%)</b>
RT	4	2 (50%)	0	<b>2 (50%)</b>

Mato, et al. ASH 2018

# Ublituximab in Multiple Sclerosis

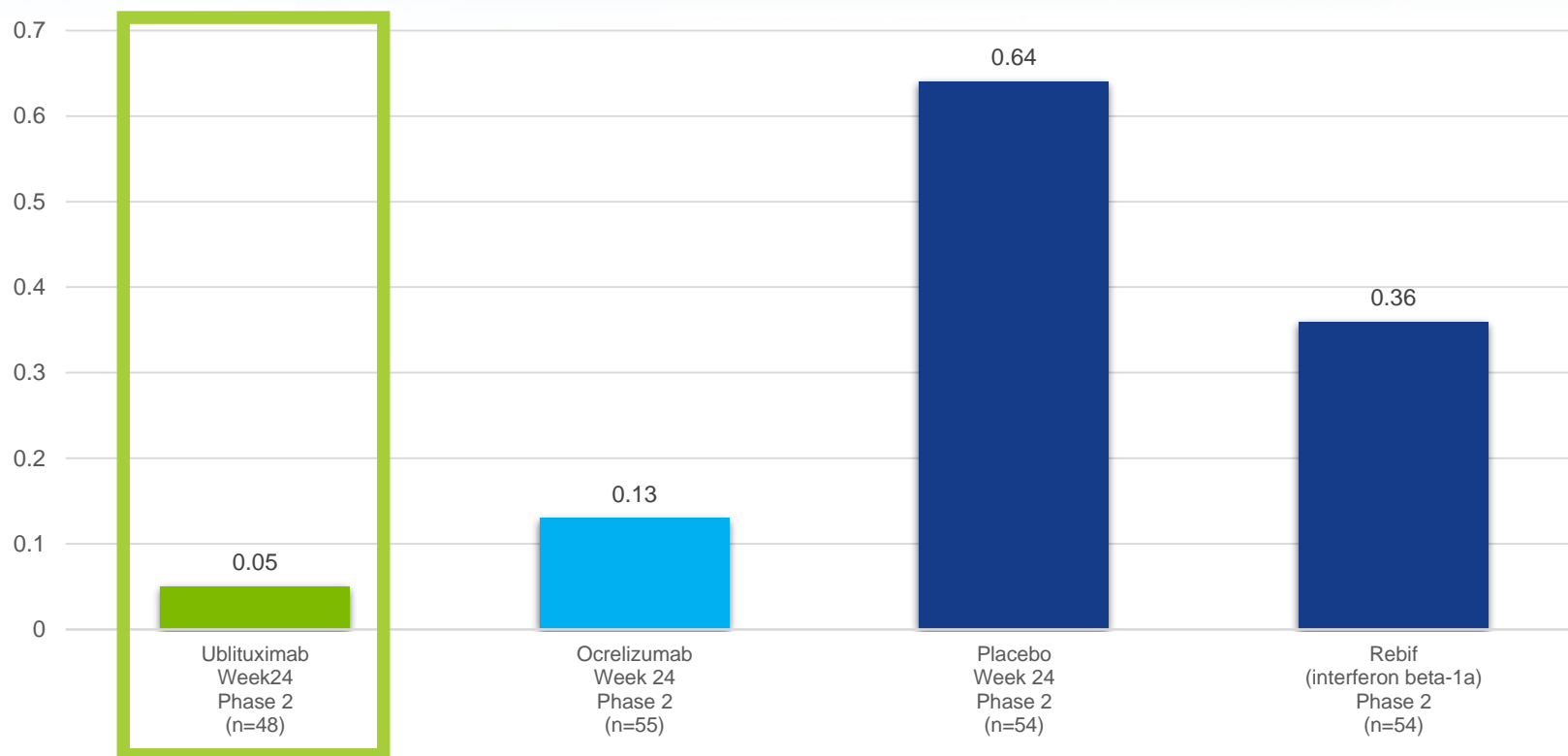
- ~1M Americans living with MS
- Completed Phase 2
- **ECTRIMS 2019:**
  - Final Phase 2 efficacy data & long-term safety data
  - First look at ULTIMATE I & II Phase 3 study design & patient demographic data



- Fully Enrolled Phase 3 ULTIMATE Trials under Special Protocol Assessment (SPA)

# MS – Phase 2 ARR Comparison

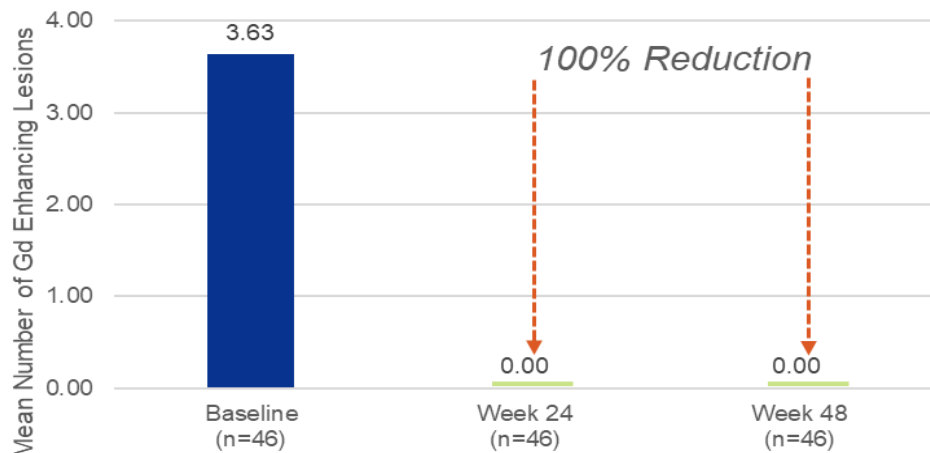
Annualized Relapse Rate (ARR) Comparator



- **Final Ublituximab Phase 2 Data at Week 48**
  - 48 patients through 48 weeks of treatment
  - Annualized Relapse Rate of .07

# Ublituximab Phase 2: MRI-Gd Enhancing Lesions

T1 Gd Enhancing Lesions Baseline vs.  
Week 24 & Week 48



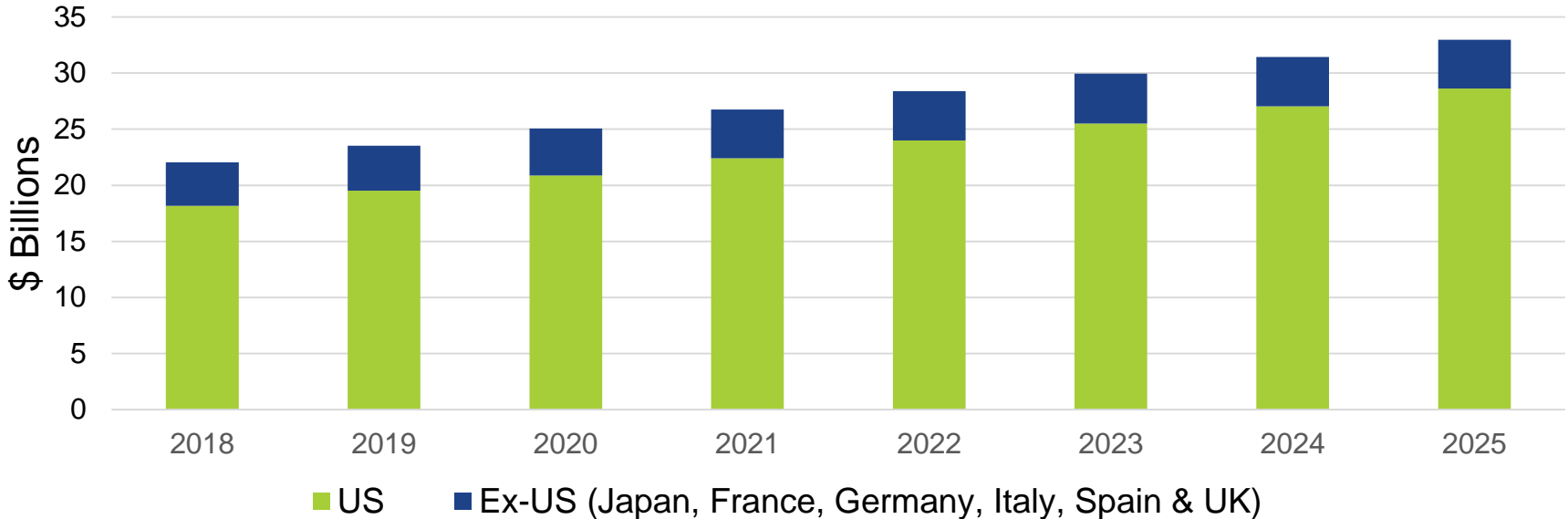
- No T1 Gd-enhancing lesions were detected in any subjects at Week 24 or Week 48 (100% reduction;  $p=0.003$ )

Subject T1 Gd MRI at Baseline, Week 24 & Week 48



# Significant Opportunity for Ublituximab in MS

Estimated Global Sales














**Global Prevalence = ~2.3Million**  
**Global Market Size >\$30Billion by 2025**

- **Current estimated ocrelizumab share: ~12% of total MS market**
- **Ocrelizumab >\$2 Billion in 2018 annual sales**

Source: Datamonitor 2018 MS Report  
Prevalence Estimate: Nat'l MS Society  
Roche JPM 2018 Corporate Update

# Multiple Treatment Options Coexist & Account for Meaningful Market Share

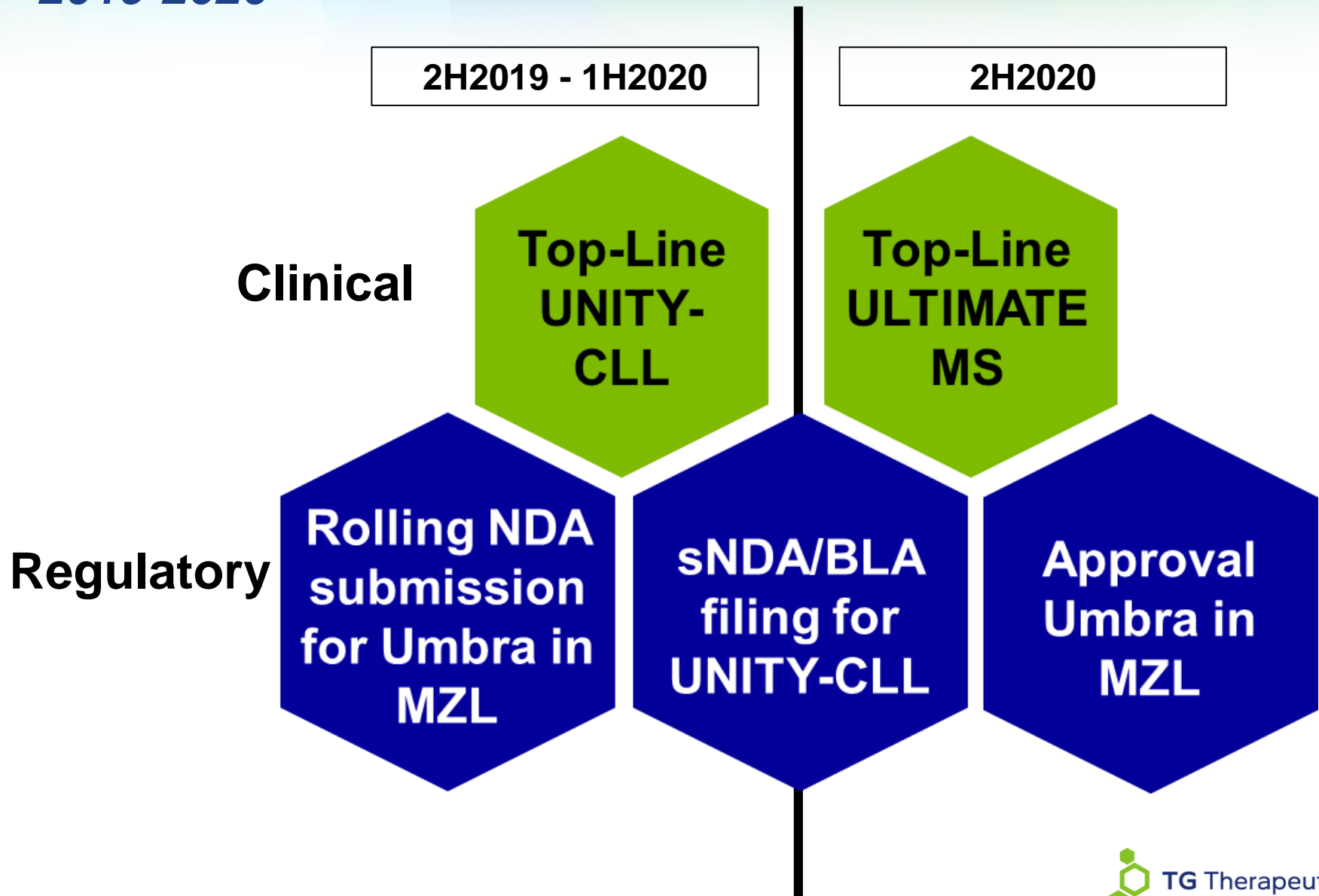
Class	Drug	U.S. Approval			Global 2018 Revenues by Drug/Class (\$ in millions)
		Date	Route of Administration	Dosing	
Interferons	 BETASERON <sup>®</sup> <small>INTERFERON BETA-1b</small>	1993	Subcutaneously	1x / 2 days	\$643
	 AVONEX <small>(interferon beta-1a)</small>	1996	Intramuscularly	1x / week	\$1,915
	 Rebif <sup>™</sup>	2002	Subcutaneously	3x / week	\$1,732
	 EXTAVIA <sup>®</sup>	2009	Subcutaneously	1x / 2 days	\$162
	 plegridy <small>(peginterferon beta-1a)</small>	2014	Subcutaneously	1x / 2 weeks	\$448
IV Potent Immunomodulators	 TYSABRI <small>(natalizumab)</small>	2004	Intravenously	1x / 4 weeks	\$1,864
	 LEMTRADA <small>(alemtuzumab)</small>	2014	Intravenously	3x / year	\$475
T-Cell Targeted Orals	 GILENYA <sup>®</sup> <small>(fingolimod)</small>	2010	Orally	1x / day	\$3,380
	 AUBAGIO <sup>®</sup> <small>(teriflunomide)</small>	2012	Orally	1x / day	\$1,945
	 Tecfidera <sup>®</sup> <small>(dimethyl fumarate)</small>	2013	Orally	2x / day	\$4,274
CD20s	 OCREVUS <sup>®</sup> <small>ocrelizumab</small>	2017	Intravenously	2x / year	\$2,406
	Ofatumumab	2020	Subcutaneously	1x / 4 weeks	TBD
	Ublituximab	2021	Intravenously	2x / year	TBD

Source: Evaluate Pharma, Wall Street Research

# Ublituximab Value Proposition in MS

- Equal to better activity with comparable safety
- Convenience of 1 hour infusion every 6 months v. 3-4 hours for Ocrelizumab
- Strategically priced to optimize patient access
- ***Estimate \$1-2B annual market opportunity in the US alone for ublituximab in MS***

# Targeted Key Data & Potential Filings/Approvals 2019-2020





# Corporate & Financial

## Key Financial Statistics

**Ticker:**

**TGTX (NASDAQ)**

**Price:**

**\$5.61 (close on 9/30/2019)**

**Shares:**

**~94.8M (fully-diluted, as of 8/2/2019)**

**Cash:**

**~\$97M (proforma as of 6/30/19)**



# TG Therapeutics

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NASDAQ: TGTX