



# **Tolerability & Durable Responses of Zandelisib Administered on an Intermittent Schedule (IS) in Relapsed/Refractory (R/R) Follicular Lymphoma (FL) and Other B-cell Malignancies**

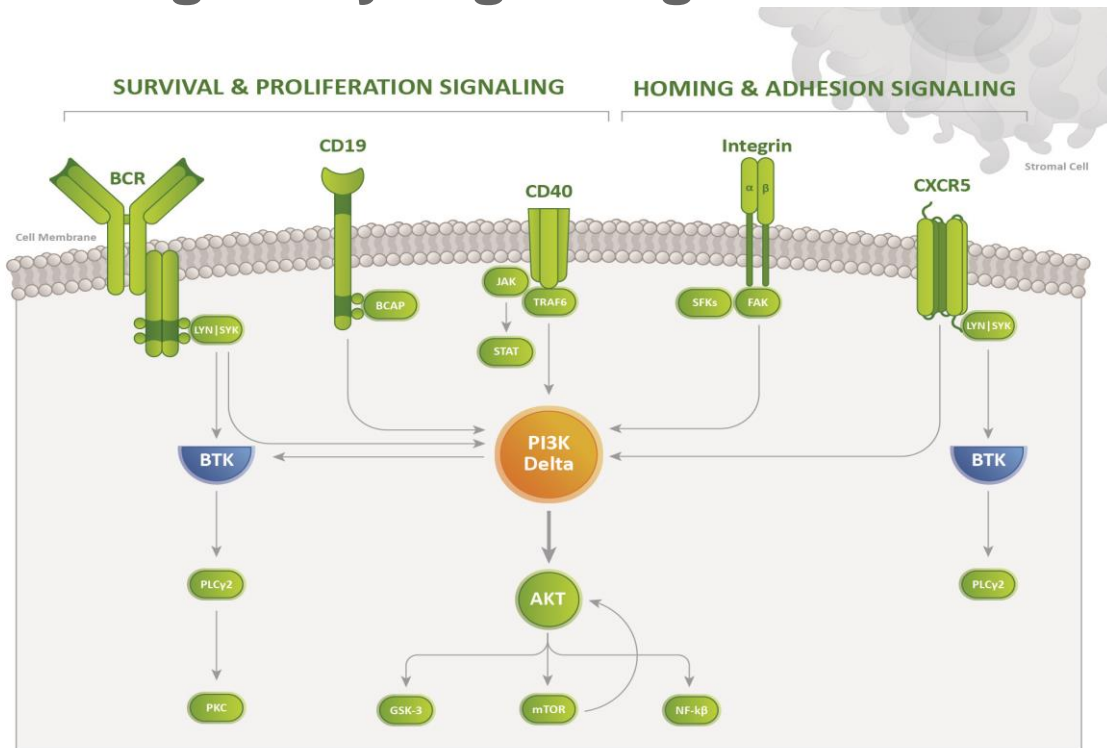
Richard Ghalie, M.D., Senior Vice President, Clinical Development,  
January 2021

# Forward-Looking Statements

- This presentation contains, and our officers and representatives may from time to time make, statements that are “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Examples of forward-looking statements include, among others, statements regarding our development strategy; potential advantages of our product candidates; the initiation and completion of preclinical and clinical studies and the reporting of the results thereof; the timing of regulatory submissions and actions; the sufficiency of our existing cash; and all other statements relating to our plans, objectives, expectations and beliefs regarding future performance, operations, financial condition and other future events (including assumptions underlying or relating to any of the foregoing).
- These forward-looking statements rely on a number of assumptions concerning future events and are subject to a number of risks, uncertainties, and other factors, many of which are outside of our control. Important factors that could cause our actual results and financial condition to differ materially from those indicated in forward-looking statements include, among others: uncertainties relating to the initiation and completion of preclinical and clinical studies; whether preclinical and clinical study results will validate and support the safety and efficacy of our product candidates; the outcome of regulatory reviews of our product candidates; varying interpretation of research and development and market data; the impact of the COVID-19 pandemic on our industry and individual companies, including on our counterparties, the supply chain, the execution of our clinical development programs, our access to financing and the allocation of government resources; risks and uncertainties relating to intellectual property and the other factors discussed under the caption “Item 1A. Risk Factors” in our most recent annual report on Form 10-K and our most recent quarterly report on Form 10-Q.
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# Zandelisib (ME-401): Targeting a Mechanism at a Crossroads of B-cell Malignancy Signaling

- PI3K $\delta$  is highly expressed in lymphoid cells and is critical for the survival, proliferation and homing of malignant B cells
- Zandelisib is an oral, once-daily, selective inhibitor of PI3K $\delta$  in clinical development for the treatment of B-cell malignancies

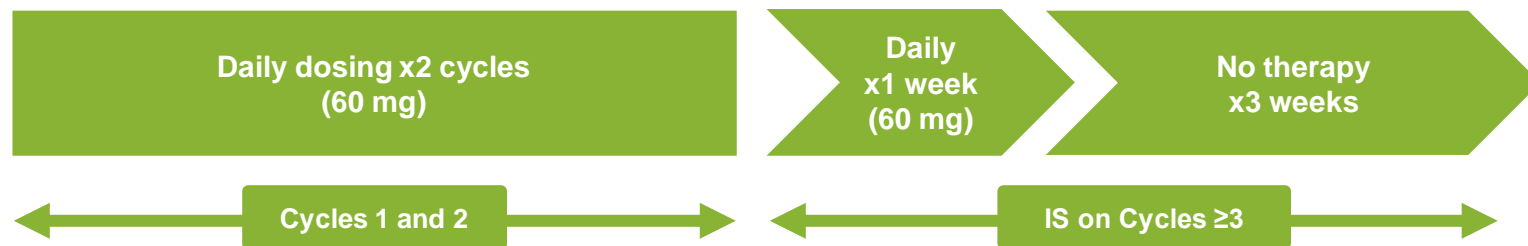


# Zandelisib Phase 1b Study: Key Findings

- **Zandelisib on the Intermittent Schedule (IS) has a high response rate and is well tolerated in R/R FL and CLL/SLL**
  - ORR = 83% in FL and 89% in CLL/SLL
  - Low incidence of Grade  $\geq 3$  AEsI
  - No Grade  $\geq 3$  AEsI reported after Cycle 3
  - Discontinuation rate due to adverse events = 7%
- **Median DOR in FL is not reached with a median follow-up 13.2 months**
  - Durable responses regardless of prior lines of therapy, treatment group ( $\pm$  rituximab) or tumor bulk

# Zandelisib Phase 1b Study

- Phase 1b dose escalation/expansion study with safety and tolerability endpoints\*
  - Main Eligibility Criteria: ECOG 0–2, failure of  $\geq 1$  prior therapy for B-cell malignancies, measurable disease, no prior PI3K or BTK therapy
- 57 patients treated on Intermittent Schedule (IS) beginning in Cycle 3
- Treatment groups: 60 mg daily as monotherapy / 60 mg in combination with rituximab



**IS used as a strategy to mitigate delayed immune-related toxicities associated with continuous daily administration of oral PI3K inhibitors**

# Patient Characteristics

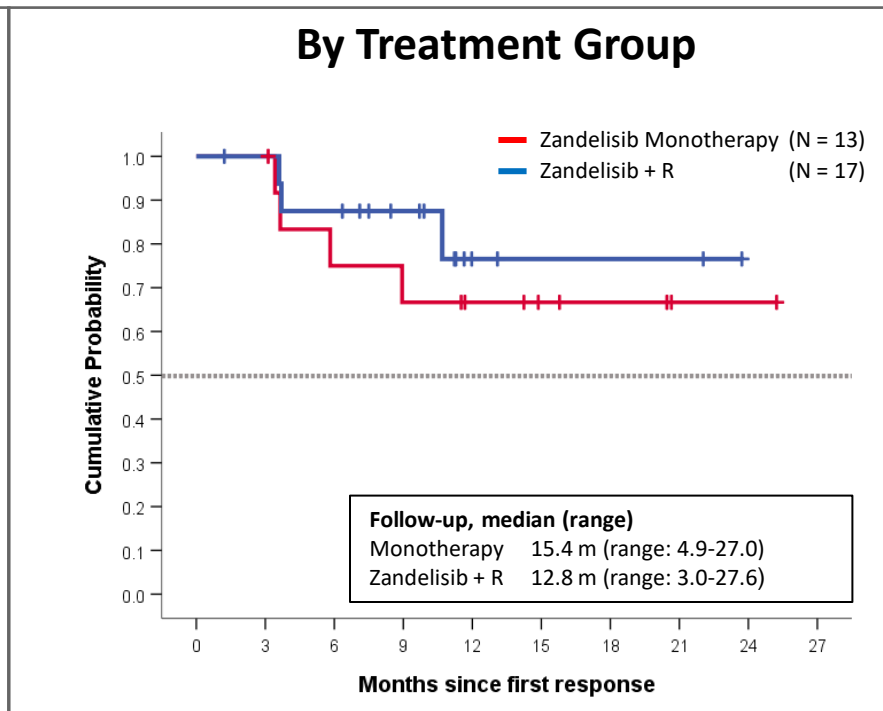
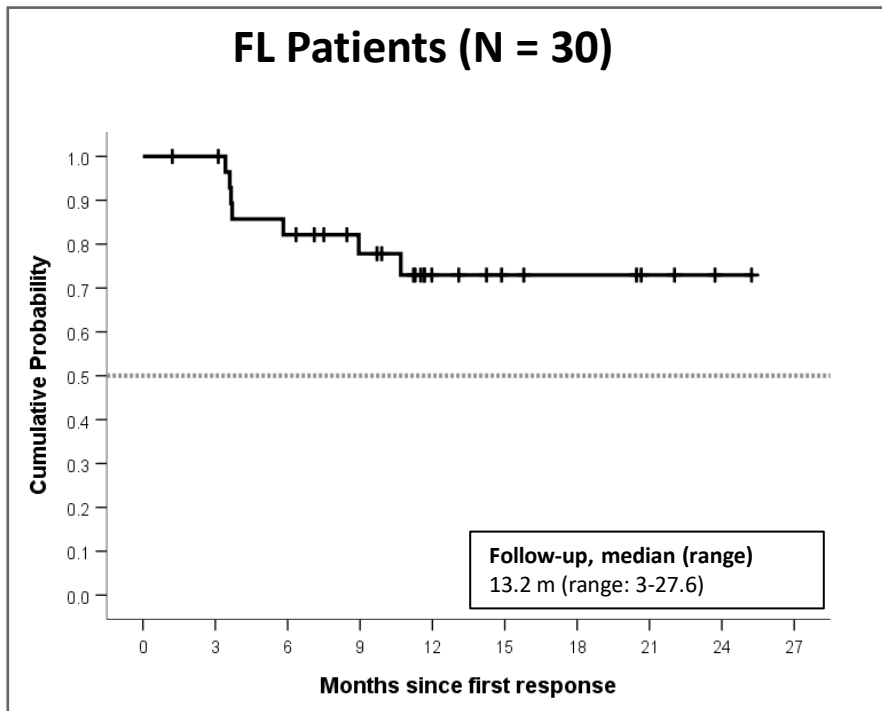
	<b>FL N=36</b>	<b>CLL N=10</b>	<b>MZL N=4</b>	<b>DLBCL N=7</b>	<b>Total N=57</b>
<b>Age</b>					
Median (range), in years	62 (38-87)	71 (46-80)	73 (70-94)	69 (60-84)	66 (38-94)
≥ 65 years, No. (%)	16 (44%)	8 (80%)	4 (100%)	6 (86%)	34 (60%)
<b>Prior anti-lymphoma therapy</b>					
Median (range)	2 (1-5)	2 (1-3)	1 (1-1)	2 (1-8)	2 (1-8)
≥ 2 prior lines	20 (56%)	5 (50%)	0	6 (86%)	31 (54%)
Prior anti-CD20 antibody	36 (100%)	9 (90%)	4 (100%)	7 (100%)	56 (98%)
<b>Diameter of largest tumor size</b>					
≥ 5 cm	19 (53%)	4 (40%)	1 (25%)	2 (29%)	26 (46%)

# Overall Responses in R/R FL

<b>Diagnosis</b>	<b>Evaluable Subjects (N)</b>	<b>ORR N (%)</b>	<b>CR Rate N (%)</b>
FL all patients	36	30 (83%)	8 (22%)
By treatment group			
Zandelisib monotherapy	17	13 (76%)	4 (24%)
Zandelisib + rituximab	19	17 (89%)	4 (21%)
By prior lines of therapy			
1 prior	16	13 (81%)	3 (19%)
≥ 2 prior	20	17 (85%)	5 (25%)

Response criteria : Lugano

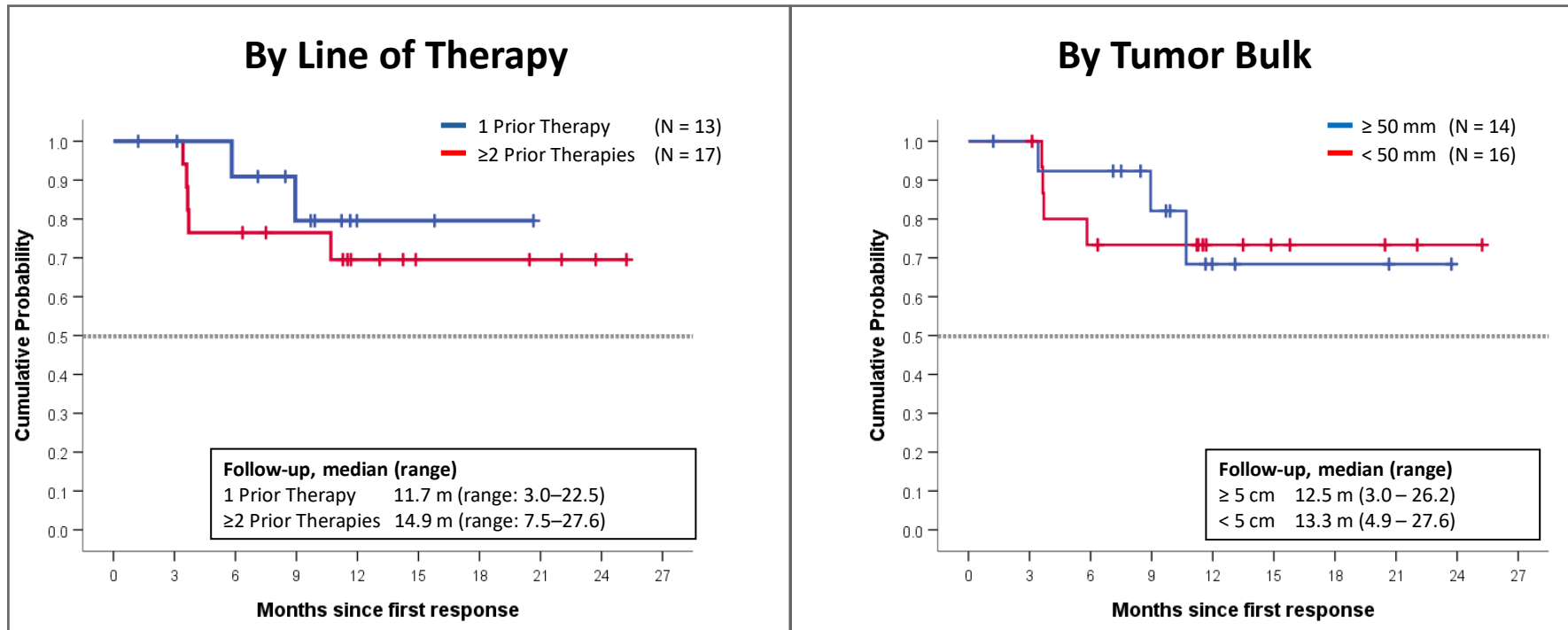
# Duration of Response in FL



Follow-up = Time from first day on study to treatment discontinuation or data cutoff date



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# Overall Response in Other R/R B-Cell Malignancies

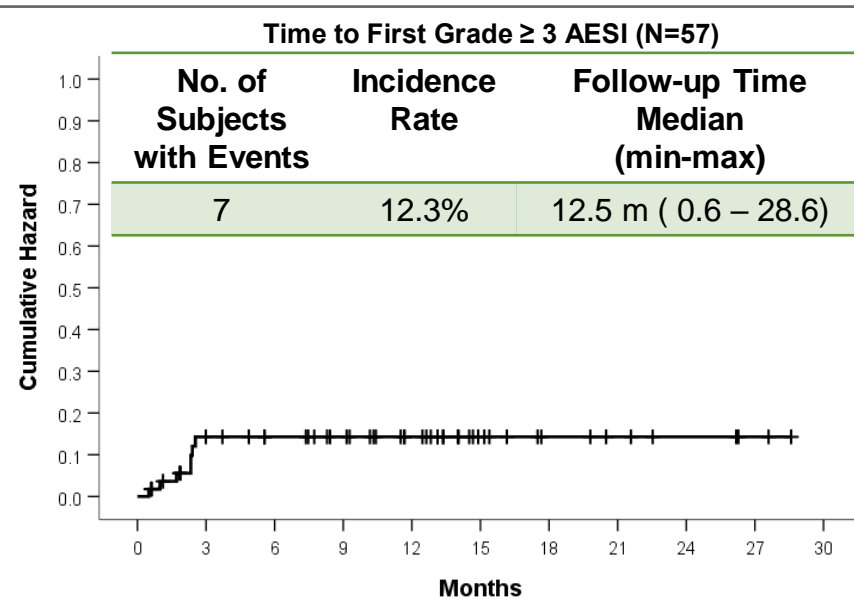
Diagnosis	Evaluable Subjects (N)	ORR N (%)	CR Rate N (%)
CLL/SLL	9	8 (89%)	1 (11%)
Zandelisib monotherapy	3	3 (100%)	0
Zandelisib + rituximab	6	5 (83%)	1 (17%)
MZL			
Zandelisib + rituximab	4	4 (100%)	1 (25%)
DLBCL			
Zandelisib + rituximab	6	1 (17%)	1 (17%)

Response criteria : iwCLL for CLL, Lugano for MZL and DLBCL

# Low Incidence of AESI: No Increased Toxicity Over Time

Adverse Events of Special Interest (AESI)	Grade 3
Diarrhea	
Diarrhea	2 (3.5%)
Colitis	2 (3.5%)
Rash, all Types	1 (1.8%)
ALT/AST elevation	1 (1.8%)
Stomatitis	0
Pneumonia / Infectious pneumonitis	0*
Non-infectious pneumonitis	1 (1.8%)

\*1 patient with Grade 5 Covid-19 pneumonia in Cycle 15 not included



- All Grade 3 AESI occurred in Cycles 1-3
- No Grade 4 AESI

- Discontinuations due to AEs in 4 patients (7%)

# Low Incidence of Grade 3-4 Myelosuppression and AST/ALT Elevation Based on Laboratory Tests

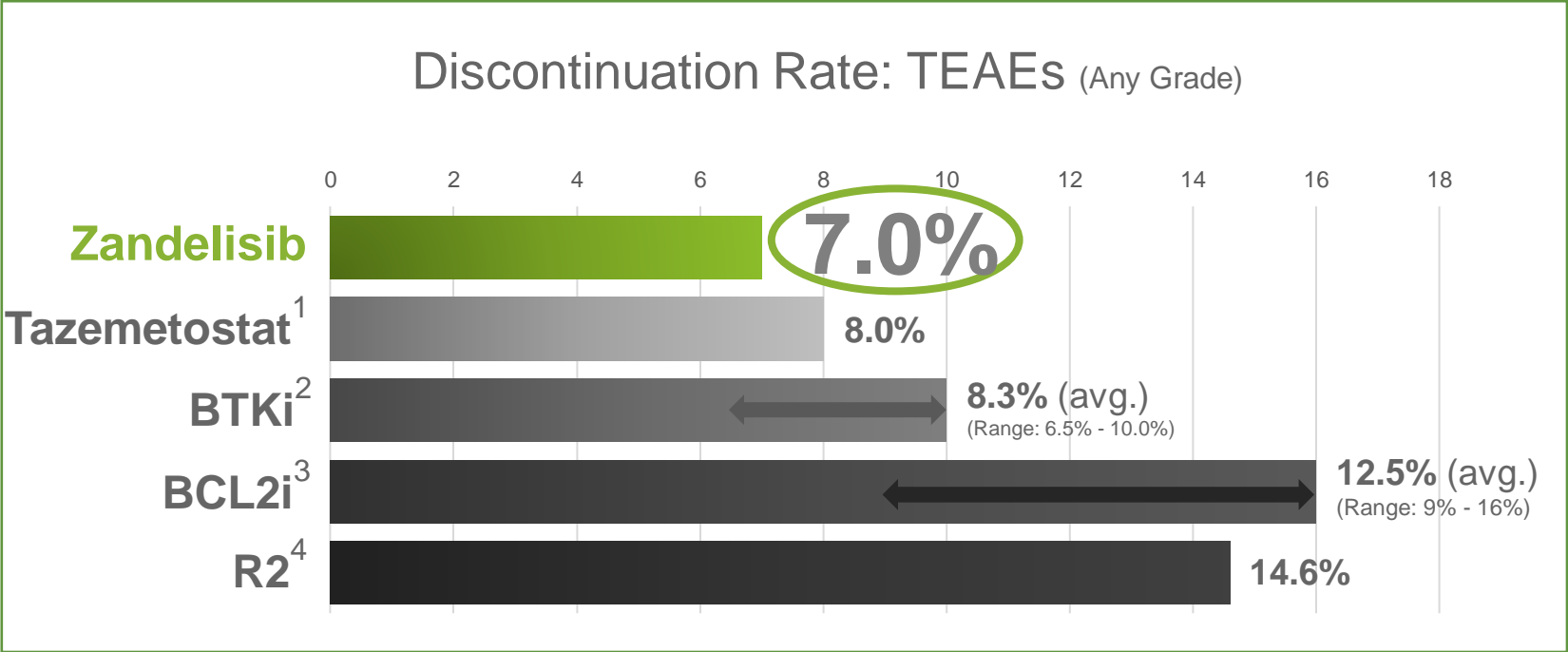
<b>Grade ≥ 3</b>	<b>Zandelisib Monotherapy (N=21)</b>	<b>Zandelisib + Rituximab (N=36)</b>	<b>Total (N = 57)</b>
<b>Increased Transaminases</b>			
AST	0 (0.0%)	0 (0.0%)	0 (0.0%)
ALT	0 (0.0%)	2 (5.6%)	2 (3.5%)
<b>Hematology</b>			
Neutropenia	3 (14.3%)	8 (22.2%)	11 (19.3%)
Anemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Thrombocytopenia	0 (0.0%)	2 (5.6%)	2 (3.5%)

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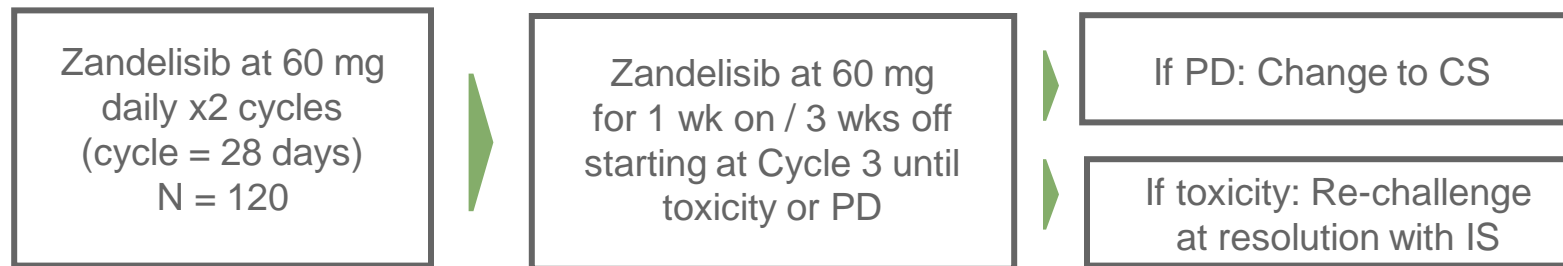
# Zandelisib Emerging Profile: Potential for Broad Acceptance Across B-Cell Malignancies & Supports Combinations with Other Modalities



1. Rate of discontinuation due to an adverse reaction from the FDA label for Tazemetostat as indicated for the treatment of follicular lymphoma (n=99). 2 Includes the FDA approved BTK inhibitors: IMBRUVICA (ibrutinib), CALQUENCE® (acalabrutinib) and BRUKINSA® (zanubrutinib). Rates of discontinuation due to an adverse reaction are from the FDA labels for IMBRUVICA (n=1,124), CALQUENCE (n=1,029) and BRUKINSA (n=629), across clinical trials evaluating patients with CLL/SLL, MCL, WM, and MZL. 3. Rates of discontinuation due to an adverse reaction are from the FDA label for VENCLIXTA (Venetoclax®) as indicated for the treatment CLL/SLL (n=758). 4. Rate of discontinuation due to an adverse reaction is from the FDA label for Revlimid® (lenalidomide) as indicated for the treatment of follicular lymphoma and marginal zone (AUGMENT trial: n=176).

Note: These data are based on cross-trial comparisons and not based on any head-to-head preclinical studies or clinical trials. As a result, the values shown may not be directly comparable and do not report robust comparative analyses. Zandelisib data is from an ongoing Phase 1b study evaluating patients on the intermittent schedule as a monotherapy or in combination with Rituxan® (rituximab). Data cutoff is April 13, 2020

# Phase 2 TIDAL Trial to Support Accelerated Approval Marketing Application – The Initial Opportunity in R/R FL



- Histologically confirmed diagnosis of FL, Grade 1, 2, or 3a
- FL, relapsed or refractory to 2 prior systemic therapies including an anti-CD20 antibody and chemotherapy
- No prior therapy with PI3K $\delta$  inhibitors
- No histological transformation to an aggressive lymphoma

# Expanding Zandelisib Development Activities to Explore Full Potential

- TIDAL study arm evaluating zandelisib monotherapy as  $\geq 3^{\text{rd}}$  line therapy in marginal zone lymphoma (MZL)
- Phase 3 study evaluating zandelisib + rituximab as  $\geq 2^{\text{nd}}$  line therapy in R/R FL and MZL
- Expanding evaluation of combination with zanubrutinib into disease specific B-cell malignancy cohorts
- Japan registrational Phase 2 study evaluating zandelisib monotherapy in R/R indolent B-cell lymphoma
- Selective IIT's (e.g., zandelisib + R-CHOP as  $1^{\text{st}}$  line therapy in DLBCL at the Cleveland Clinic)

**Exploration of other indications and combinations are also part of the extended development plan with Kyowa Kirin**



# Zandelisib

*Conclusion*

## Zandelisib: Regaining the Promise of PI3K $\delta$

**Differentiated  
Profile Results in  
Best-in-class  
Potential**

**Potential to Meet  
Need Across  
Multiple B-cell  
Malignancies**

**Multiple  
Combination  
Regimen  
Opportunities**



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