

BeiGene



BeiGene

***EHA Update on BTK Inhibitor Zanubrutinib  
and the Clinical Development Program***

*June 15, 2018*

# Forward Looking Statements

Certain statements contained in this presentation, other than statements of fact that are independently verifiable at the date hereof, may constitute forward-looking statements. Examples of such forward-looking statements include those regarding investigational drug candidates and clinical trials and the status and related results thereto, as well those regarding continuing and further development and commercialization efforts. Such statements, based as they are on the current analysis and expectations of management, inherently involve numerous risks and uncertainties, known and unknown, many of which are beyond BeiGene's control. Such risks include but are not limited to: the impact of general economic conditions, general conditions in the pharmaceutical industries, changes in the global and regional regulatory environments in the jurisdictions in which BeiGene does business, market volatility, fluctuations in costs and changes to the competitive environment. Consequently, actual future results may differ materially from the anticipated results expressed in the forward-looking statements. In the case of forward-looking statements regarding investigational drug candidates and continuing further development efforts, specific risks which could cause actual results to differ materially from BeiGene's current analysis and expectations include: failure to demonstrate the safety, tolerability and efficacy of our drug candidates, final and quality controlled verification of data and the related analyses, the expense and uncertainty of obtaining regulatory approval, including from the FDA, CFDA and EMA, and the possibility of having to conduct additional clinical trials. Further, even if regulatory approval is obtained, pharmaceutical products are generally subject to: stringent on-going governmental regulation, challenges in gaining market acceptance and competition. These statements are also subject to a number of material risks and uncertainties that are described in BeiGene's filings with the Securities and Exchange Commission. The reader should not place undue reliance on any forward-looking statements included in this presentation. These statements speak only as of the date made, and BeiGene is under no obligation and disavows any obligation to update or revise such statements as a result of any event, circumstances or otherwise, unless required by applicable legislation or regulation.

Clinical data in this presentation relating to BeiGene's investigational drug candidates is from early phase, single-arm trials. When such data are presented in relation to other investigational or marketed drug products, the presentation and discussion are not based on head-to-head trials between BeiGene's investigational drug candidates and other products. BeiGene is still conducting clinical trials and, as additional patients are enrolled and evaluated, data on BeiGene's investigational drug candidates may change.

This presentation and the accompanying oral presentation contains data and information obtained from third-party studies and internal company analysis of such data and information. BeiGene has not independently verified the data and information obtained from these sources. Forward-looking information obtained from these sources is subject to the same qualifications noted above.

# Agenda

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- Opening Remarks and Introduction, John Oyler, CEO of BeiGene
- EHA 2018 Data Review by Dr. Jane Huang, CMO for Hematology, BeiGene
  - *Abstract # PS1186: Improved Depth of Response with Increased Follow-Up for Patients (PTS) with Waldenström Macroglobulinemia (WM) Treated with Bruton's Tyrosine Kinase (BTK) Inhibitor Zanubrutinib*
  - *Abstract # PF445: Pooled Analysis of Safety Data from Zanubrutinib (BGB-3111) Monotherapy Studies in Hematologic Malignancies*
- Zanubrutinib Development Update, Dr. Eric Hedrick, Chief Advisor, BeiGene
- Q&A with BeiGene Management Team

# BeiGene Company Introduction

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**Fully-integrated biopharmaceutical company with late-stage clinical candidates and commercial products, poised to capture program-based opportunities globally and leverage regulatory reforms in China**

- Founded in Beijing in 2010 initially as an R&D organization focused on developing best-in-class oncology therapeutics and has evolved into a fully-integrated biopharmaceutical company
  - Global team with more than 1,100 employees in China, the US and Australia
  - Full capabilities from research, development, manufacturing to sales and marketing in China
  - Strong global oncology development organization of 450+, over 200 each in the U.S. and APAC
  - Fourteen pivotal or potentially registration-enabling trials ongoing for three late-stage assets with three marketed oncology products in China and a robust pipeline
- Poised to realize two significant, program-based opportunities
  - Globally commercialize zanubrutinib, a potentially best-in-class BTK inhibitor
  - Develop and successfully commercialize tislelizumab, a PD-1 inhibitor, in a rapidly and favorably evolving China market by leveraging the Celgene collaboration
- Well positioned to take advantage of the regulatory reforms in China for global development

# BeiGene Product Portfolio and Pipeline

Three marketed products in China; 14 pivotal or potentially registration-enabling trials ongoing for three late-stage assets

Program (Target)	Commercial Rights	Dose Esc		Dose Exp		Pivotal		Lead Indications
		Phase 1a	Phase 1b	Phase 2*	Phase 2**	Phase 3		
zanubrutinib (BGB-3111, BTK)	Worldwide						<ul style="list-style-type: none"> <li>WM, 1L CLL/SLL</li> <li>R/R MCL, R/R CLL/SLL, WM</li> </ul>	
zanubrutinib + GAZYVA® (BTK + CD20)	Worldwide						<ul style="list-style-type: none"> <li>R/R FL</li> </ul>	
tislelizumab (BGB-A317, PD-1)	Worldwide for hem malignancy, Asia ex-Japan for solid tumors <sup>1</sup>						<ul style="list-style-type: none"> <li>2L NSCLC, 1L HCC, 2L ESCC</li> <li>R/R HL (Pivotal phase 2), 2L+ UC (Pivotal phase 2)</li> <li>2L/3L HCC, R/R NK/T-cell lymphomas</li> </ul>	
tislelizumab + pamiparib (PD-1 + PARP)	Worldwide						<ul style="list-style-type: none"> <li>Solid tumors</li> </ul>	
tislelizumab + zanubrutinib (PD-1 + BTK)	Worldwide						<ul style="list-style-type: none"> <li>B-cell malignancies</li> </ul>	
pamiparib (BGB-290, PARP)	Worldwide <sup>2</sup>						<ul style="list-style-type: none"> <li>Solid tumors</li> <li>3L gBRCA+ ovarian cancer</li> <li>2L plat-sensitive ovarian cancer maintenance</li> </ul>	
pamiparib + TMZ (PARP + Chemo)	Worldwide <sup>2</sup>						<ul style="list-style-type: none"> <li>Solid tumors</li> </ul>	
pamiparib + RT/TMZ (PARP + RT/Chemo)	Worldwide <sup>2</sup>						<ul style="list-style-type: none"> <li>Glioblastoma</li> </ul>	
lifirafenib (BGB-283, RAF Dimer)	Worldwide <sup>2</sup>						<ul style="list-style-type: none"> <li>B-Raf- or K-RAS/N-RAS-mutated solid tumors</li> <li>B-Raf- or K-RAS/N-RAS-mutated solid tumors</li> </ul>	
BGB-A333 +/- tislelizumab (PD-L1 +/- PD-1)	Worldwide						<ul style="list-style-type: none"> <li>Solid tumors</li> </ul>	
REVLIMID® (IMiD)***	China	Marketed					<ul style="list-style-type: none"> <li>R/R MM (marketed), NDMM (marketed), R/R NHL (Phase 3)</li> </ul>	
ABRAXANE® (Albumin-bound paclitaxel)	China	Marketed					<ul style="list-style-type: none"> <li>Breast cancer</li> </ul>	
VIDAZA® (hypomethylating agent)	China	Marketed					<ul style="list-style-type: none"> <li>MDS, AML with 20-30% bone marrow blasts, CMMoL</li> </ul>	
CC-122 (CELMoD)	China	Planned					<ul style="list-style-type: none"> <li>R/R DLBCL and NHL</li> </ul>	
sitravatinib (multi-kinase inhibitor)	Asia ex-Japan, AU, NZ <sup>3</sup>	Planned					<ul style="list-style-type: none"> <li>NSCLC</li> </ul>	

\*Some indications will not require a non-pivotal Phase 2 clinical trial prior to beginning pivotal Phase 2 or 3 clinical trials. \*\*Confirmatory clinical trials post approval are required for accelerated approvals. \*\*\*Revlimid approved as a combination therapy with dexamethasone. <sup>1</sup>Celgene has the right to develop and commercialize tislelizumab in solid tumors in the United States, European Union, Japan and the rest-of-world outside of Asia. <sup>2</sup>Limited collaboration with Merck KGaA. <sup>3</sup>Partnership with Mirati Therapeutics, Inc.



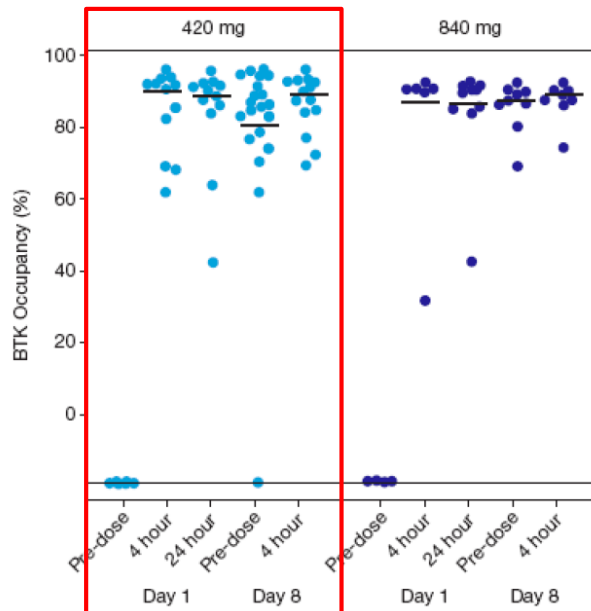
# Introduction to Zanubrutinib

- Bruton's tyrosine kinase (BTK) plays a critical role in B-cell receptor (BCR) signaling, which mediates B-cell proliferation, migration, and adhesion<sup>1-3</sup>
  - *The BCR pathway is an established therapeutic target in multiple subtypes of non-Hodgkin's lymphoma (NHL)*<sup>4,5</sup>
- Based on preclinical data, zanubrutinib was shown to be a potent, highly selective, and irreversible BTK inhibitor, with greater selectivity for BTK vs. other TEC- and EGFR-family kinases and demonstrated favorable pharmacokinetic properties, including superior oral bioavailability compared to ibrutinib
- Zanubrutinib achieved complete and sustained BTK occupancy in peripheral blood mononuclear cells and lymph nodes in patients treated at 160 mg BID<sup>6</sup>

# Ibrutinib: Target Inhibition Appears Incomplete and Compartment-Dependent

Clinical data show borderline target inhibition by ibrutinib in the blood at approved dose

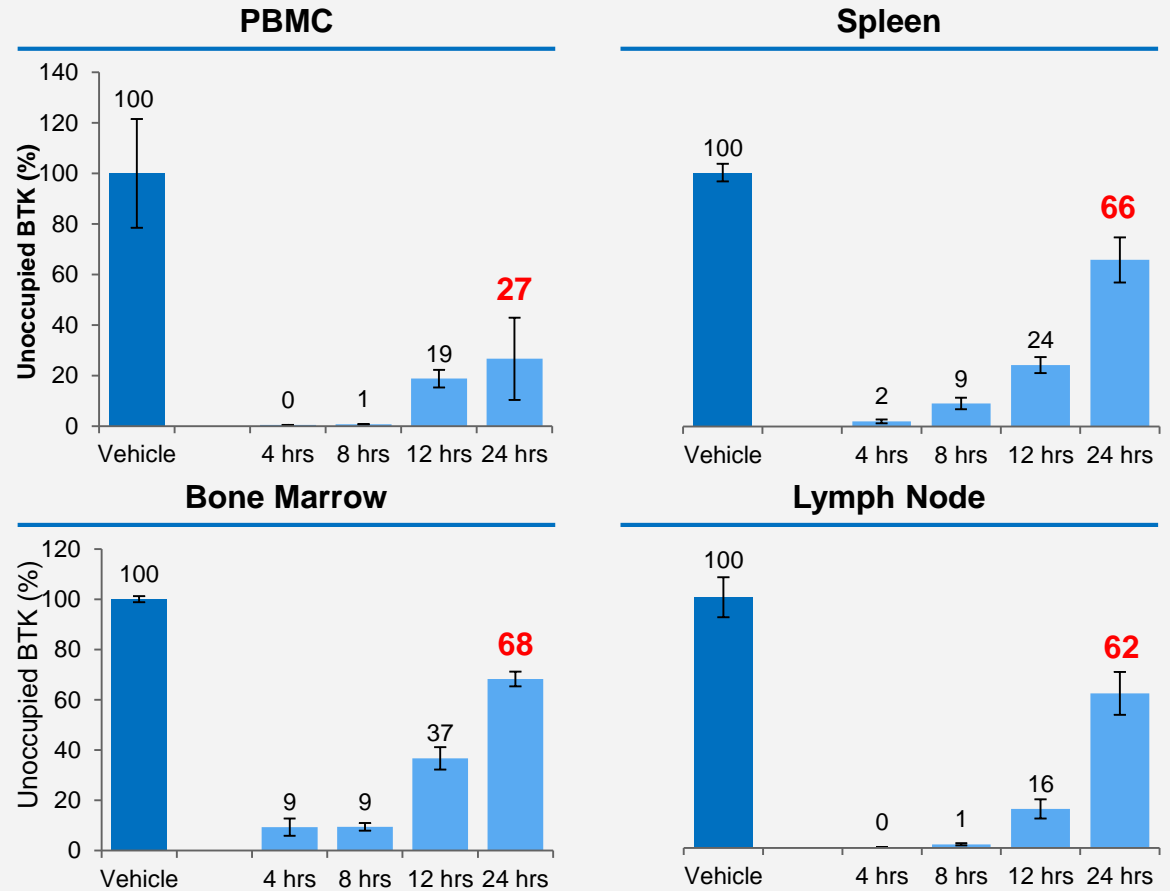
## Ibrutinib Clinical Data in Blood



Approved Ibrutinib Doses: 420mg for CLL and WM; 560mg for MCL

Byrd et al., NEJM, 2013

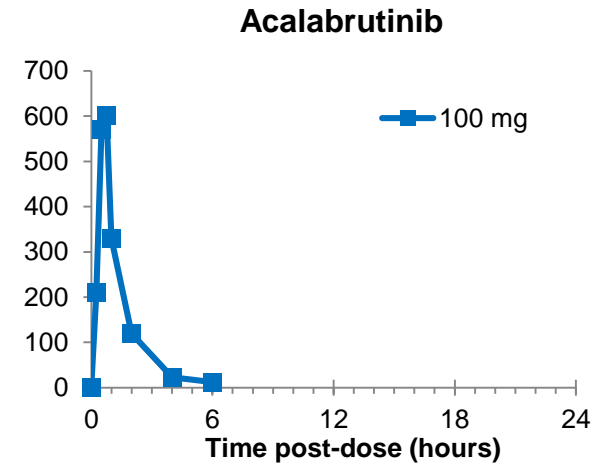
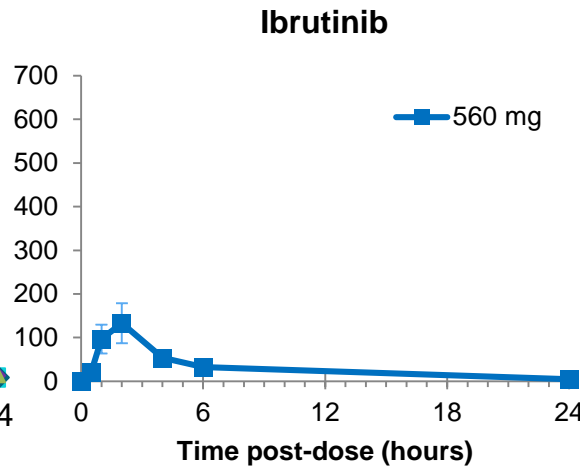
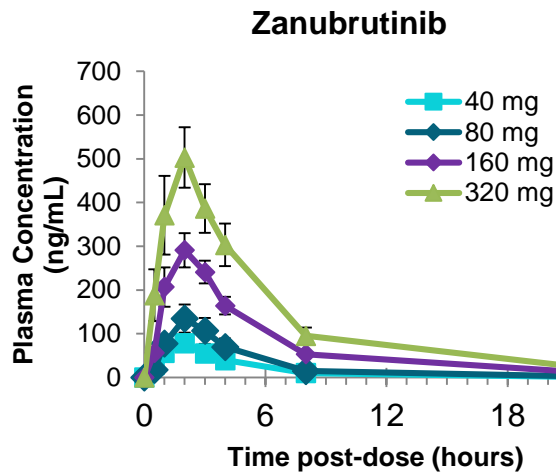
Preclinical models\* show significant recovery of target occupancy in disease relevant tissues for ibrutinib



Note: PBMC = Peripheral Blood Mononuclear Cell; Source: BeiGene data and Byrd et al, NEJM, 2013

\*Animal studies

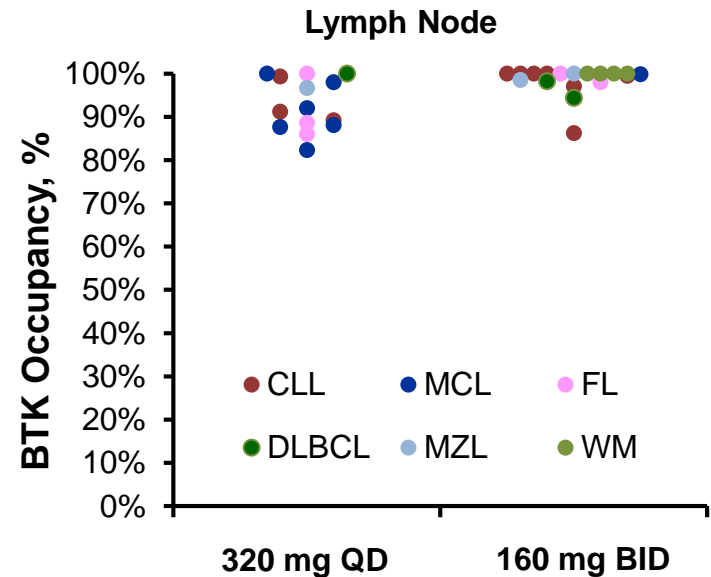
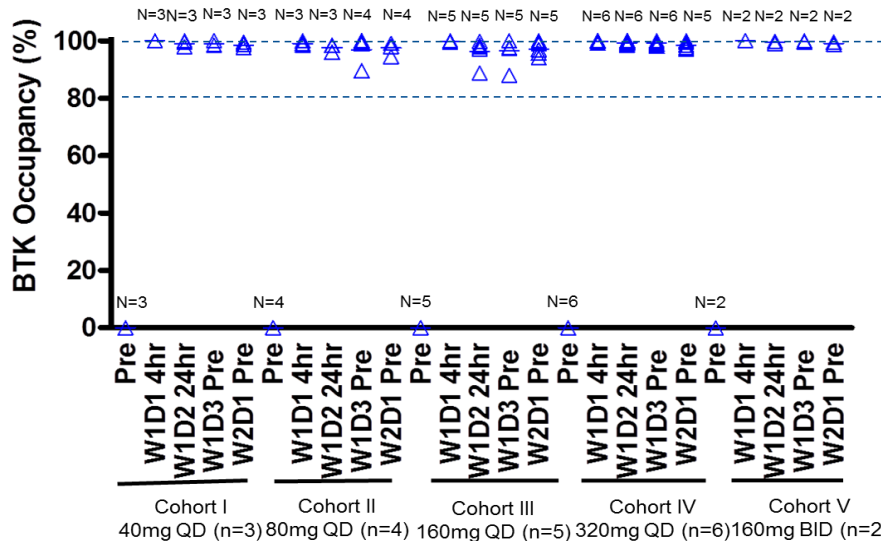
# Zanubrutinib: Pharmacokinetic Profile and Sustained BTK Occupancy in Blood and Lymph Node



Adapted from Advani, et al, *J Clin Oncol*, 2013

Adapted from Byrd et al., *NEJM*, 2015

PBMC



Data are from independent studies

Source: <sup>1</sup>Tam CS, et al. *Blood*. 2015;126:832. <sup>2</sup>Advani RH, et al. *J Clin Oncol*. 2013;31:88-94. <sup>3</sup>Byrd, et al. *NEJM*. 2016;374:323-32. <sup>4</sup>Tam, et al. ASH 2016 (Abstracts 642 and 1216)





# Agenda

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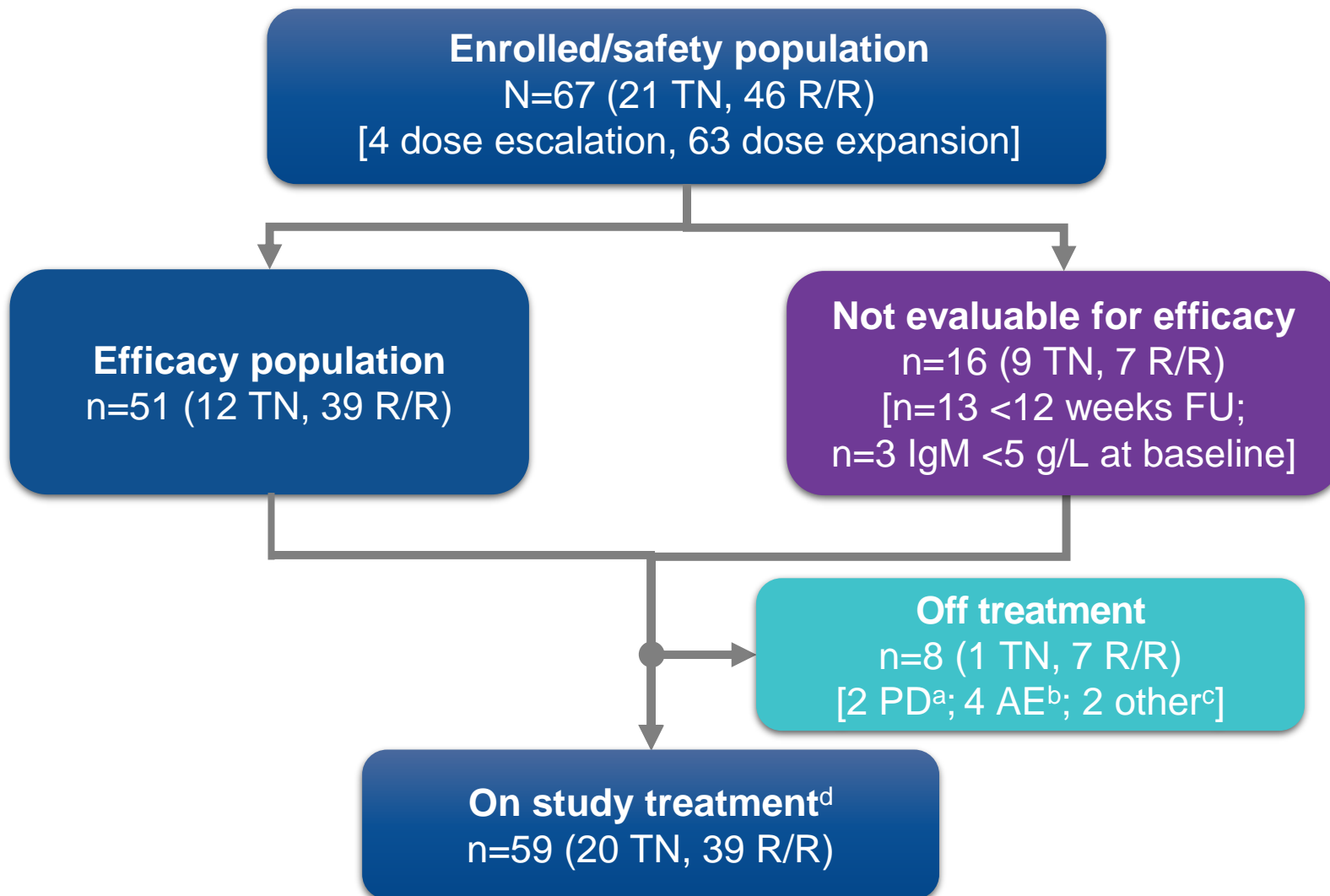
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- **EHA 2018 Data Review by Dr. Jane Huang, CMO for Hematology, BeiGene**
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# Improved Depth of Response With Increased Follow-Up For Patients With Waldenström Macroglobulinemia (WM) Treated With Bruton's Tyrosine Kinase Inhibitor Zanubrutinib (BGB-3111)

Judith Trotman,<sup>1,2</sup> Constantine S Tam,<sup>3,4,5,6</sup> Paula Marlton,<sup>7,8</sup> David Gottlieb,<sup>9</sup> David Simpson,<sup>10</sup> Gavin Cull,<sup>11,12</sup> David Ritchie,<sup>3,4,6</sup> Emma Verner,<sup>1</sup> Javier Munoz,<sup>13</sup> Sumita Ratnasingam,<sup>14</sup> Mary Ann Anderson,<sup>2,4,6</sup> Peter Wood,<sup>7,8</sup> Eric Hedrick,<sup>15</sup> Jane Huang,<sup>15</sup> Sunhee Ro,<sup>15</sup> James Hilger,<sup>15</sup> John F Seymour,<sup>3,4,6</sup> Andrew W Roberts,<sup>4,6</sup> Stephen Opat<sup>14,16</sup>

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# WM: Patient Disposition\*



\*As of November 3, 2017;

<sup>a</sup>Week 24 after SD, Week 49 after PR; <sup>b</sup>Worsening Bronchiectasis, prostate adenocarcinoma, gastric adenocarcinoma, acute myeloid leukemia;

<sup>c</sup>Radiation/ transplant, noncompliance, secondary malignancy;

<sup>d</sup>One patient post PD still on treatment.

AE, adverse event; FU, follow-up; PD, progressive disease; R/R, relapsed/refractory; TN, treatment-naïve.

# Patient and Disease Characteristics

Characteristics	WM Total (N=67)
Age, years, median (range)	66 (44-87)
ECOG Performance Status, n(%)	
0	24 (36)
1	41 (61)
2	2 (3)
Prior treatment status	
Treatment-naïve, n (%)	21 (31)
Relapsed/refractory, n (%)	46 (69)
Number of prior therapies, median (range)	2 (1-8)
Prior anti-CD20 treatment, n (% of R/R)	43 (93)
Genotype, n (%)	
<i>MYD88</i> <sup>L265P</sup> / <i>CXCR4</i> <sup>WT</sup>	28 (42)
<i>MYD88</i> <sup>L265P</sup> / <i>CXCR4</i> <sup>WHIM</sup>	5 (7)
<i>MYD88</i> <sup>WT</sup>	8 (12)
Unavailable	26 (39)

# Overall Response in WM

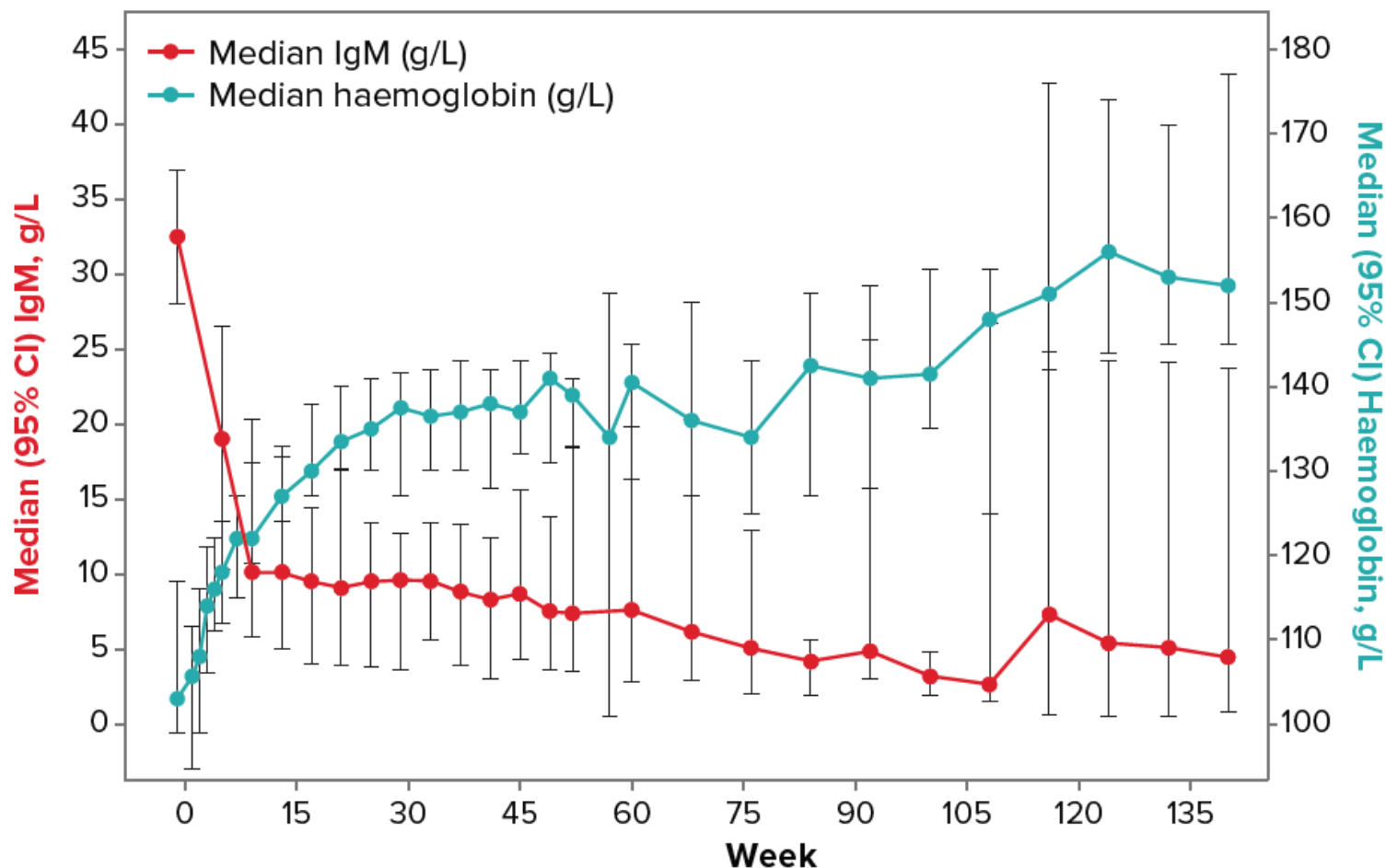
Best Response in WM	Zanubrutinib
Enrolled (evaluable for efficacy), n	67 (51)
Median follow up	16.9 months
Response Criteria	Modified 6 <sup>th</sup> IWWM
ORR, n (%)	47 (92%)
MRR	41 (80%)
<b>VGPR</b>	<b>22 (43%)</b>

Source: Trotman et al., EHA 2018

# Best Response Overall and MYD88 Mutations Status

Best response, n (%)	OVERALL (n=51)	By MYD88 Status			
		<i>MYD88</i> <sup>L265P</sup> / <i>CXCR4</i> <sup>WT</sup> (n=25)	<i>MYD88</i> <sup>L265P</sup> / <i>CXCR4</i> <sup>WHIM</sup> (n=5)	<i>MYD88</i> <sup>WT</sup> (n=6)	Unknown Status (n=15)
ORR	47 (92)	23 (92)	5 (100)	5 (83)	14 (93)
MRR	41 (80)	21 (84)	4 (80)	3 (50)	13 (87)
<b>VGPR</b>	<b>22 (43)</b>	<b>14 (56)</b>	<b>2 (40)</b>	<b>1 (17)</b>	<b>5 (33)</b>
PR	19 (37)	7 (28)	2 (40)	2 (33)	8 (53)
MR	6 (12)	2 (8)	1 (20)	2 (33)	1 (7)
SD	4 (8)	2 (8)	0	1 (17)	1 (7)

# Changes in IgM and Hemoglobin Over Time (evaluatable patients, n=51)

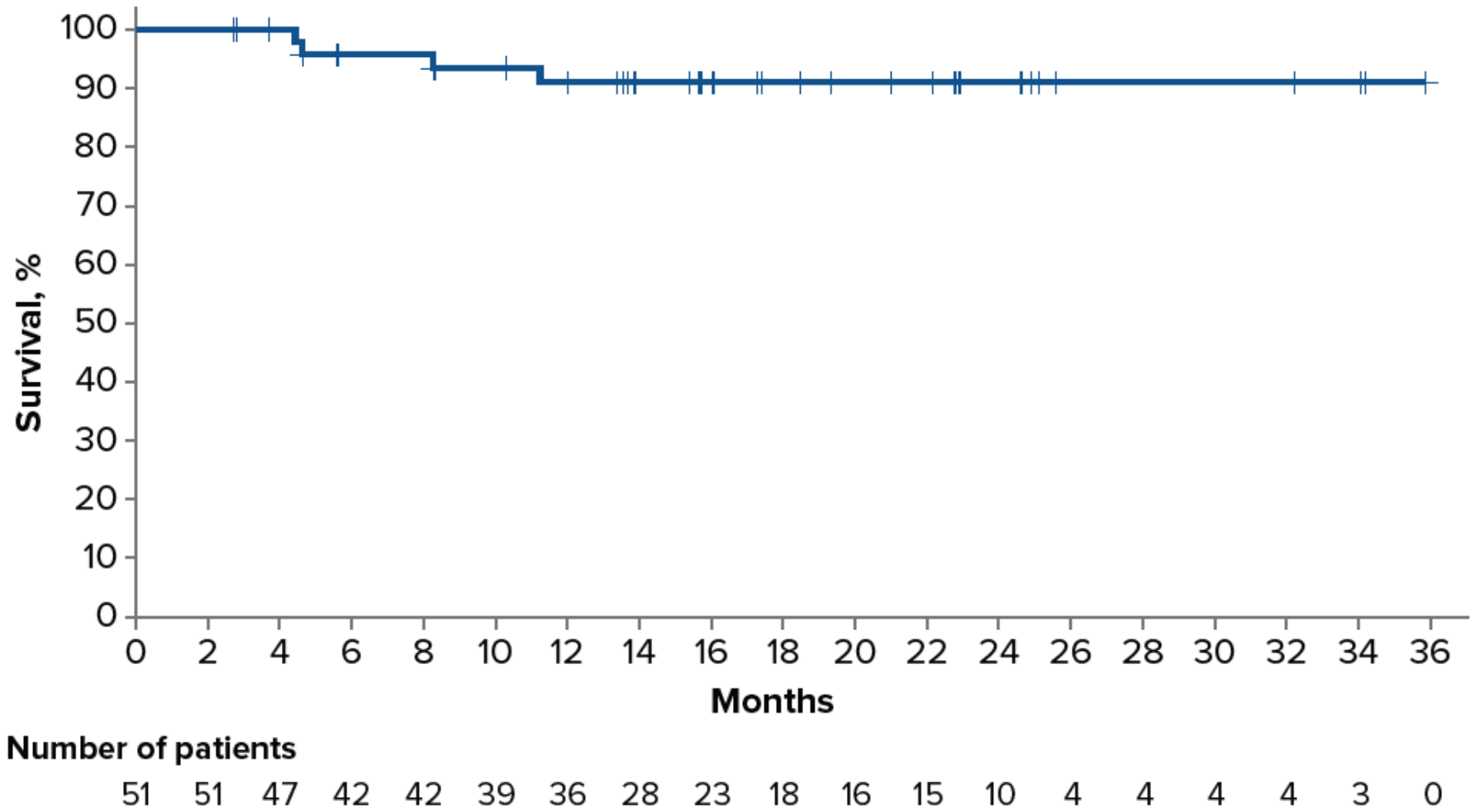


## Number of patients

IgM	51	50	49	45	43	39	39	33	34	28	22	17	16	13	10	4	4	4	4
Haemoglobin,	51	44	51	46	42	42	40	37	38	29	23	18	17	14	10	4	4	4	4

Note: patient numbers shown only at timepoints with data for both IgM and hemoglobin.

# Progression-Free Survival in Evaluable Patients (n=51)





# Most Common Adverse Events of Any Attribution

Adverse Event	N=67		Adverse Event	N=67	
	All Gr %	Gr 3-4 %		All Gr %	Gr 3-4 %
Petechiae/purpura/ contusion	37		Gastroesophageal reflex disease	10	
Upper respiratory tract infection	34		Neutropenia	10	6.0
Constipation	18		Rash	10	
<b>Diarrhea</b>	18	1.5	Basal cell carcinoma	9.0	3.0
Cough	13		Hypertension	9.0	3.0
Anemia	12	7.5	Squamous cell carcinoma	6.0	3.0
Back pain	12	3.0	<b>Atrial fibrillation/flutter</b>	6.0	
Epistaxis	12		Pyrexia	4.5	3.0
Headache	12	1.5	Pneumonia	4.5	3.0
Nausea	12		Actinic keratosis	4.5	3.0
Urinary track infection	12		<b>Major hemorrhage*</b>	<b>3.0</b>	<b>3.0</b>

BTK inhibitor events of interest are in bold. AEs of interest chosen based on warnings and precautions for other BTK inhibitors.

Common AEs include all grade  $\geq 10\%$  or grade 3-4  $\geq 2\%$ .

\*Grade  $\geq 3$  hemorrhage, or CNS hemorrhage of any grade. The most common AEs in patients with WM were primarily grade 1-2 in severity.

# Adverse Events of Interest

Event, n (%)	n (%)
Patients with $\geq 1$ AE Grade $\geq 3$	26 (38.8%)
Patients with $\geq 1$ serious AE*	22 (32.8%)
Events leading to treatment discontinuation <sup>†</sup>	4 (6.0%)
<b>AE of special interest, n (%);</b>	
Grade $\geq 3$ Diarrhea	1 (1.5%)
Major hemorrhage <sup>‡</sup>	2 (3.0%)
Grade $\geq 3$ Atrial fibrillation	0 (0%)

\*SAEs possibly related to zanubrutinib were hemothorax, atrial fibrillation, colitis, febrile neutropenia, and headache (each n=1).

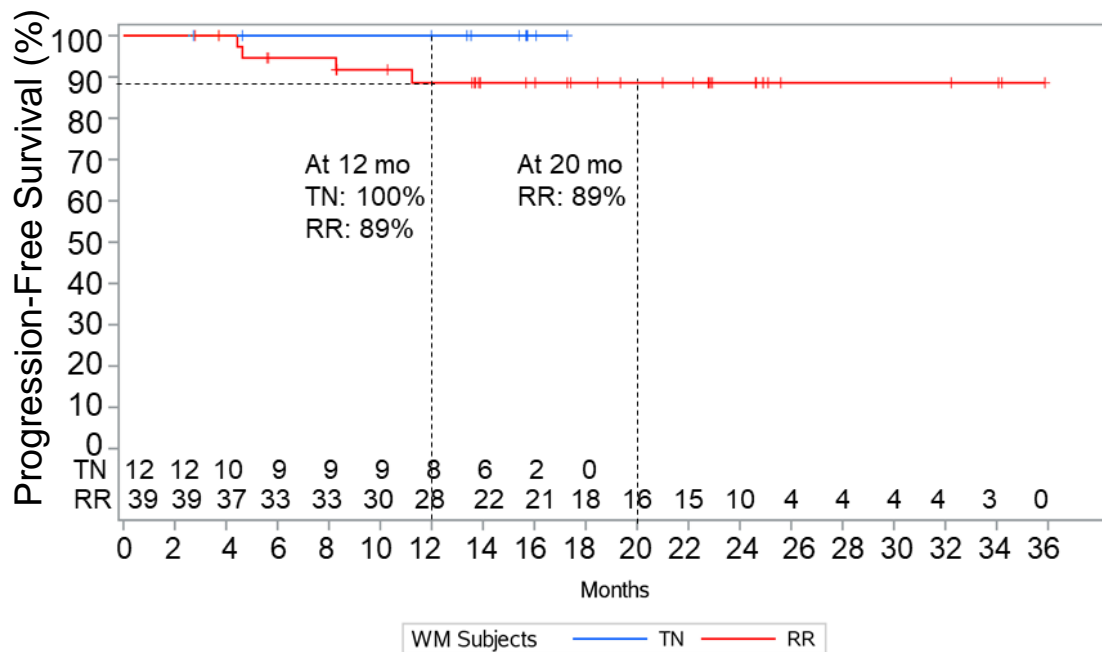
<sup>†</sup>Worsening bronchiectasis (fatal), gastric adenocarcinoma, prostate adenocarcinoma, acute myeloid leukemia (n=1 each).

<sup>‡</sup>Major hemorrhage (any grade  $\geq 3$  hemorrhage or any grade CNS hemorrhage) was reported in 2 patients (3%, both grade 3-4);

Atrial fibrillation/flutter was reported in 4 patients (6%; 0 grade 3-4).

# Zanubrutinib in WM: Response Rate and Progression-Free Survival

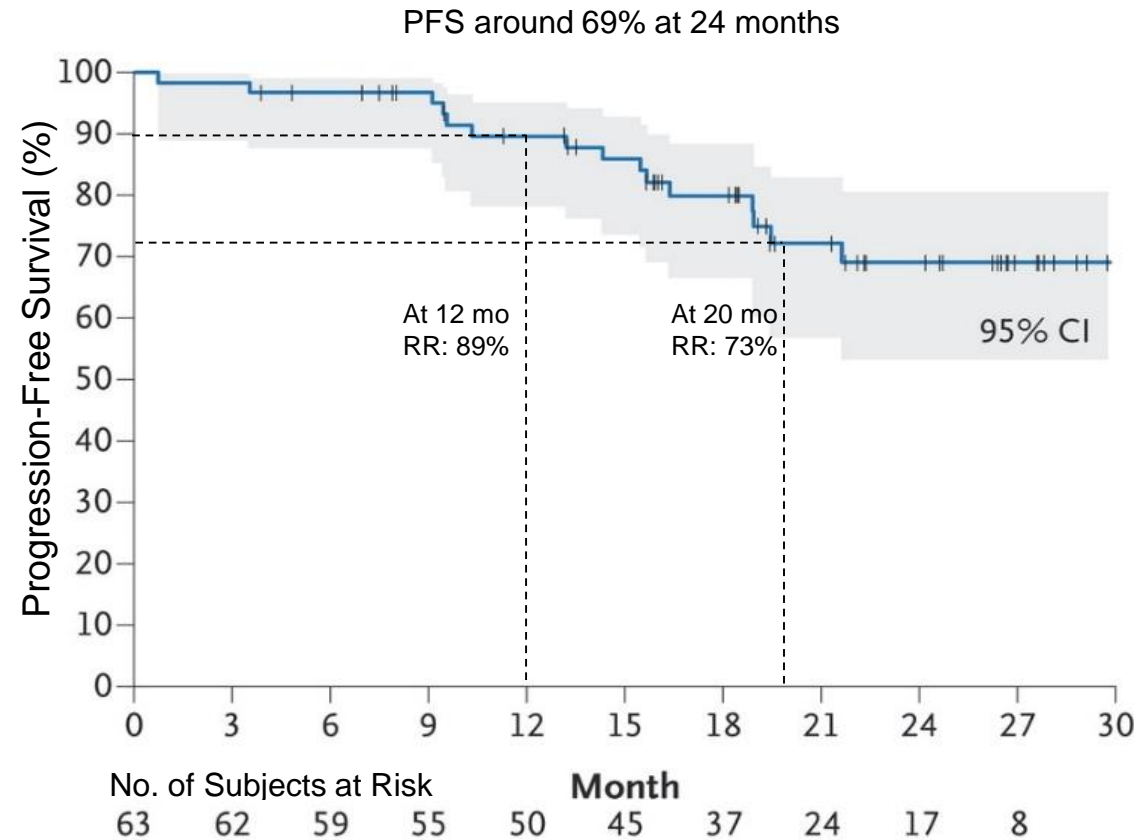
Among 51 evaluable patients, 91% remained progression free at 12 months



Zanubrutinib EHA 2018	TN	R/R	Overall
Criteria	Modified IWWM-3 (IgM only)		
mFU (range)	16.9 mos (3.1 – 37.6)		
n	12	39	51
ORR	12 (100%)	35 (90%)	47 (92%)
MRR	10 (83%)	31 (80%)	41 (80%)
<b>VGPR</b>	<b>4 (33%)</b>	<b>18 (46%)</b>	<b>22 (43%)</b>
PR	6 (50%)	13 (33%)	19 (37%)
MR	2 (17%)	4 (10%)	6 (12%)
SD	0	4 (10%)	4 (8%)
Median IgM Reduction (g/L)			32.5 to 4.9 (85%)
Median Hb Change* (g/dl)			8.7 to 13.8

\*Of 22 efficacy evaluable patients (43%) with hemoglobin <10 g/dL at baseline, the median increased from 8.7 g/dL (range, 6.3-9.8) to 13.8 g/dL (range, 7.7-15.8).

# Ibrutinib in WM: Response Rate and Progression-Free Survival



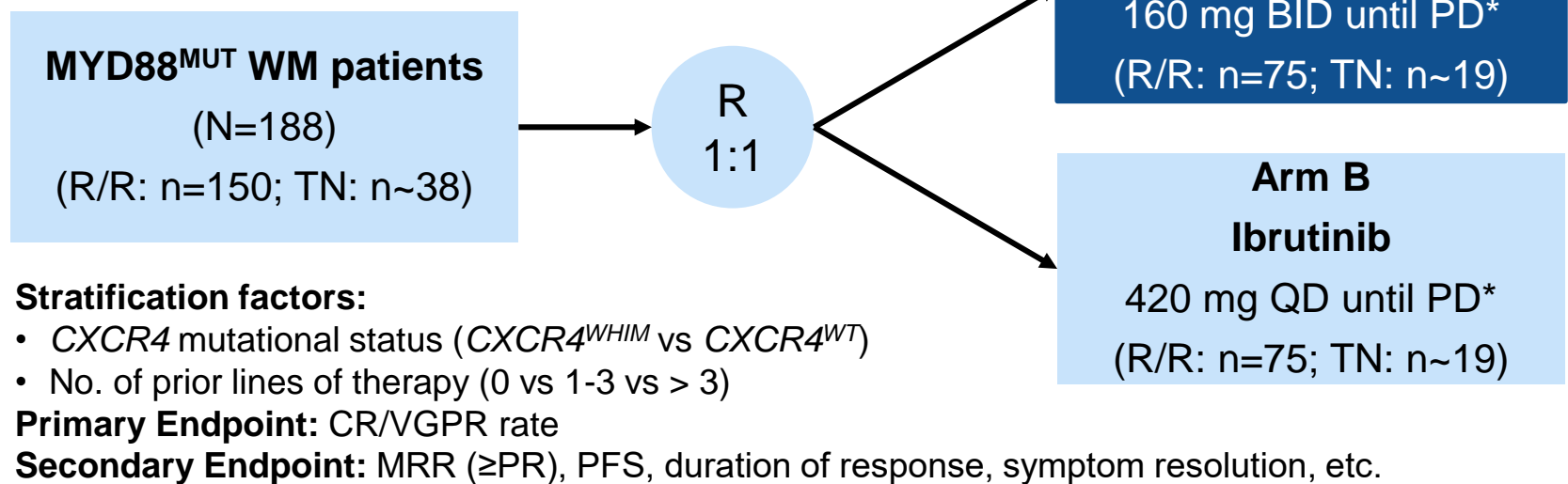
Ibrutinib NEJM 2015	R/R
Criteria	Modified IWWM-3 (IgM only)
mDOT (range)	19.1mo (0.5-29.7)
N	63
PFS (24 mos)	69%
ORR	57 (90%)
MRR	46 (73%)
<b>VGPR</b>	<b>10 (16%)</b>
PR	36 (57%)
MR	11 (17%)
SD	6 (10%)
Median IgM Reduction (g/L)	35.2 to 8.8 (75%)
Median Hb Change* (g/dl)	105 to 138

DOT=Duration of Treatment  
Source: Treon *et al.*, NEJM, 2015

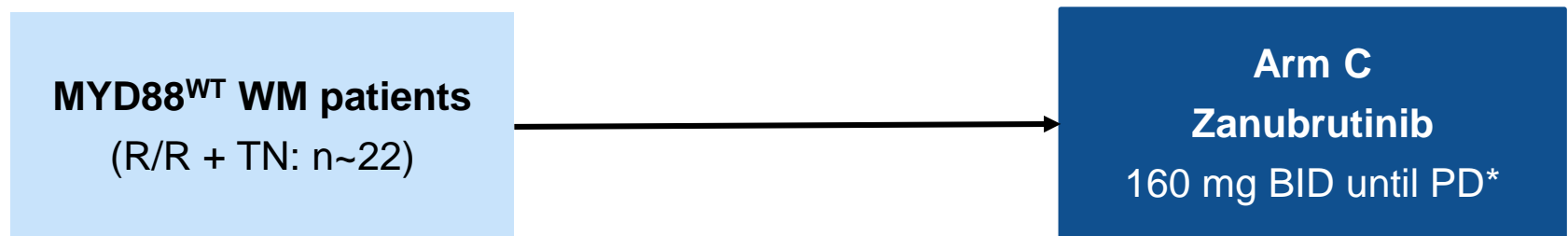
# BGB-3111-302: Waldenströms Phase 3 Trial Design

## Cohort 1: R/R or TN<sup>^</sup> WM with *MYD88* mutation

<sup>^</sup>TN must be unsuitable for standard chemoimmunotherapy



## Cohort 2: WM with wild type *MYD88*; present in ~10% of enrolled patients



This study is registered at ClinicalTrials.gov (NCT03053440)

\*Until progressive disease, unacceptable toxicity, death, withdrawal of consent, or study termination by sponsor

# Pooled Analysis of Safety Data from Zanubrutinib (BGB-3111) Monotherapy Studies in Hematologic Malignancies

Constantine S Tam,<sup>1,2,3,4</sup> Judith Trotman,<sup>5,6</sup> David Simpson,<sup>7</sup> David Ritchie,<sup>1,2,4</sup> Emma Verner,<sup>5</sup> Sumita Ratnasingam,<sup>8</sup> Mary Ann Anderson,<sup>2,4,6</sup> Peter Wood,<sup>9,10</sup> John F Seymour,<sup>1,2,4</sup> Jun Zhu,<sup>11</sup> Jianyong Li,<sup>12</sup> Paula Marlton,<sup>9,10</sup> David Gottlieb,<sup>13</sup> Leo Lin,<sup>14</sup> Sunhee Ro,<sup>14</sup> James Hilger,<sup>14</sup> Aihua Wang,<sup>14</sup> Xiajun Xu,<sup>14</sup> Meng Ji,<sup>14</sup> Andrew W Roberts,<sup>2,4</sup> Stephen Opat,<sup>8,15</sup> Gavin Cull,<sup>16,17</sup>

<sup>1</sup>Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia; <sup>2</sup>University of Melbourne, Parkville, Victoria, Australia; <sup>3</sup>St Vincent's Hospital, Fitzroy, Victoria, Australia; <sup>4</sup>Royal Melbourne Hospital, Parkville, Victoria, Australia; <sup>5</sup>Concord Repatriation General Hospital, Concord, Australia; <sup>6</sup>University of Sydney, Concord, Australia; <sup>7</sup>North Shore Hospital, Auckland, New Zealand; <sup>8</sup>Monash Health, Clayton, Victoria, Australia; <sup>9</sup>Princess Alexandra Hospital, Brisbane, Australia; <sup>10</sup>University of Queensland, Brisbane, Australia; <sup>11</sup>Beijing Cancer Hospital, Beijing, China; <sup>12</sup>Jiangsu Province Hospital, Nanjing, China; <sup>13</sup>University of Sydney, Westmead Hospital, Sydney, Australia; <sup>14</sup>BeiGene (Beijing) Co. Ltd., Beijing, China and Emeryville, CA, United States; <sup>15</sup>Monash University, Clayton, Victoria, Australia; <sup>16</sup>Sir Charles Gairdner Hospital, Perth, Australia; <sup>17</sup>University of Western Australia; Perth, Australia

# Pooled Safety Data Analysis: Zanubrutinib Monotherapy Studies

Phase	Where Conducted	Malignancies	Patients* (N)
1	China	B-cell malignancies, various	44
2	China	R/R CLL/SLL	91
2	China	R/R MCL	86
1	Australia, NZ, US, Korea, Italy	B-cell malignancies, various	255

CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; MCL, mantle cell lymphoma; R/R, relapsed/refractory.

\*All patients have been treated with  $\geq 1$  dose of oral (po) zanubrutinib at 40 mg once-daily to 160 mg twice-daily (bid).

# Patient and Disease Characteristics

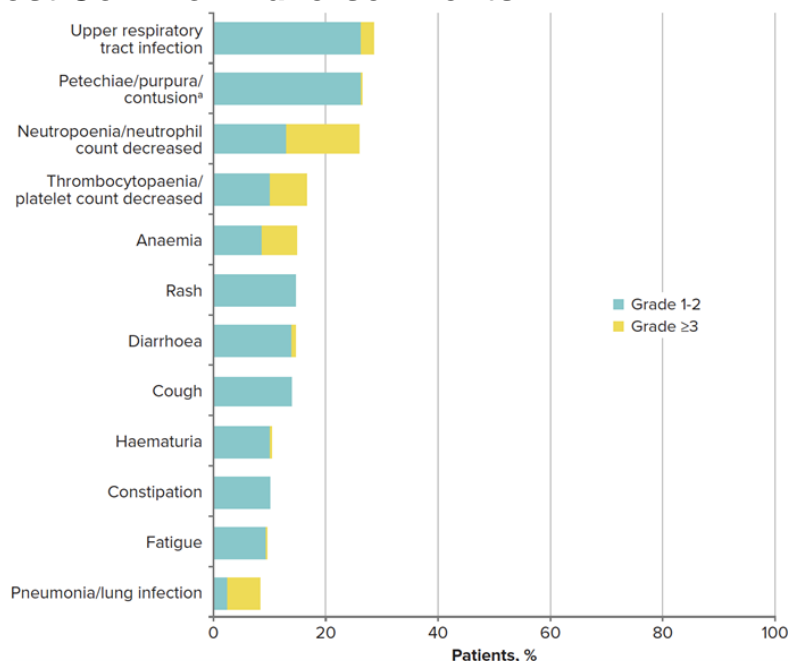
Characteristics	N=476*
Age (years), median (range)	63 (20-87)
<65 years, n (%)	266 (56)
65 to <75 years, n (%)	146 (31)
≥75 years, n (%)	64 (13)
Median treatment exposure, median (maximum)	7 months (36 months)
Male sex, n (%)	333 (70)
Female sex, n (%)	143 (30)
Eastern Cooperative Oncology Group performance status, n (%)	
0	236 (50)
1	218 (46)
2	22 (5)
Prior treatment status, n (%)	
Treatment-naïve	38 (8)
Relapsed/refractory	438 (92)
Prior lines of therapy, median (range)	2 (1-10)

\*A total of 476 patients were included in the pooled analysis, with a data cutoff date of November 3, 2017. Median age was 63 years and 70% were male. Majority of patients (92%) had relapsed/refractory disease

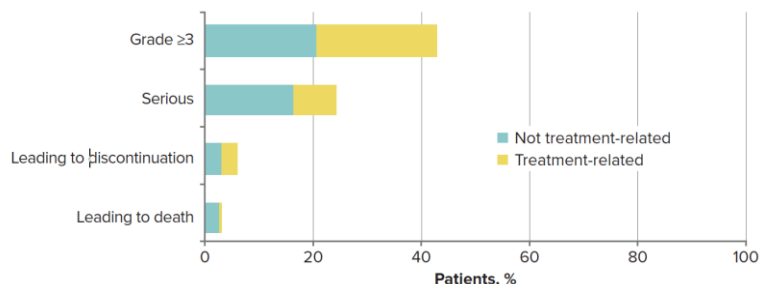


# Most Common Adverse Events of Any Attribution and Safety Summary

## A. Most Common Adverse Events\*



## B. Safety Summary



Adverse Events	N=476
Months of Exposure (med)	7.0
≥1 AE	94%
<b>Most common Grade ≥3 AEs</b>	
Neutropenia/neutrophil count decreased/febrile neutropenia	14%
Anemia	7%
Thrombocytopenia	7%
<b>Serious AEs</b>	
Zanubrutinib related	8%
Pneumonia <sup>†</sup>	6%
Pleural effusion	1%
Febrile neutropenia	1%
<b>Discontinuation due to treatment-related AEs</b>	3%

\*All Grade in ≥10% or Grade ≥3 in ≥2%. <sup>a</sup>Includes patients with any of the 3 preferred terms.

<sup>†</sup> The only treatment-related SAE reported in >1% of patients was pneumonia/ lung infection (2%).

# Summary of Adverse Events of Interest

AEs of Interest <sup>^</sup> in Patients	n (%)
Most common bleeding events	
Petechiae / purpura / contusion	126 (26.5%)
Hematuria	50 (10.5%)
Major hemorrhage <sup>†</sup>	8 (1.7%)
Fatal event related to zanubrutinib	1 (0.2%)
Atrial fibrillation <sup>‡</sup>	8 (1.7%)
Grade $\geq$ 3 diarrhea <sup>*</sup>	4 (0.8%)
Basal cell carcinoma <sup>‡</sup>	15 (3.2%)
Squamous cell carcinoma of skin	7 (1.5%)

<sup>^</sup>AEs of interest chosen based on warnings and precautions for other BTK inhibitors.

<sup>†</sup>Major hemorrhage included gastrointestinal hemorrhage / melena (n=3), cerebral hemorrhage, haematuria, purpura, haemorrhagic cystitis, renal hematoma, and hemothorax (each n=1). Among these 8 patients with major hemorrhage, only 1 had thrombocytopenia AEs or medical history of thrombocytopenia. The median time to first major hemorrhage was 1.2 months (range, 0.1-8.6).

<sup>‡</sup>Amongst patients with emergent atrial fibrillation/flutter (n=8), a majority had known risk factors including hypertension (n=2), pre-existing cardiovascular disease (n=2), and concurrent infection (n=1).

<sup>\*</sup>The cumulative rates of Grade  $\geq$ 3 infections were 14% at month 6, 19% at month 12, and 21% at month 18; Exposure-adjusted incidence rate of 1.82 per 100 person-months.

<sup>‡</sup>The most common second primary malignancies included basal cell carcinoma (3%) and squamous cell carcinoma of skin (2%); Other Grade  $\geq$ 3 second primary malignancies included breast cancer, colon cancer, invasive ductal breast carcinoma, lentigo maligna, lung neoplasm malignant, malignant melanoma, metastases to central nervous system, and prostate cancer

# Agenda

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- Opening Remarks and Introduction, John Oyler, CEO of BeiGene
- EHA 2018 Data Review by Dr. Jane Huang, CMO for Hematology, BeiGene
  - *Abstract # PS1186: Improved Depth of Response with Increased Follow-Up for Patients (PTS) with Waldenström Macroglobulinemia (WM) Treated with Bruton's Tyrosine Kinase (BTK) Inhibitor Zanubrutinib*
  - *Abstract # PF445: Pooled Analysis of Safety Data from Zanubrutinib (BGB-3111) Monotherapy Studies in Hematologic Malignancies*
- **Zanubrutinib Development Updates, Dr. Eric Hedrick, Chief Advisor, BeiGene**
- Q&A with BeiGene Management Team

# Summary of Zanubrutinib Clinical Program

■ China 
 ■ Global (ex-China) 
 ■ Global (China included)

Program (Target)	Commercial Rights	Preclinical	Dose Escalation		Dose Expansion*		Pivotal**	
			Phase 1a	Phase 1b	Phase 2	Phase 2	Phase 3	
zanubrutinib (BGB-3111) (BTK)	Worldwide	Waldenstrom's macroglobulinemia (WM): zanubrutinib vs. ibrutinib						
		Treatment-naïve chronic lymphocytic leukemia (CLL): zanubrutinib vs. BR						
		Relapsed / Refractory (R/R) mantle cell lymphoma						
		R/R CLL/SLL						
		WM						
		R/R diffuse large B-cell lymphoma						
		B-cell malignancies						
zanubrutinib + GAZYVA® (BTK + CD20)	Worldwide	R/R follicular lymphoma: zanubrutinib + GAZYVA® vs. GAZYVA®						
		B-cell malignancies						
zanubrutinib + tislelizumab (BTK + PD-1)	Worldwide	Hematological tumors						

- More than 1,200 patients' enrolled across zanubrutinib program, including combination trials
- Additional Phase 3 comparing zanubrutinib and ibrutinib planned in patients with relapsed / refractory CLL

\*Some indications will not require a non-pivotal Phase 2 clinical trial prior to beginning pivotal Phase 2 or 3 clinical trials. \*\*Confirmatory clinical trials post approval are required for accelerated approvals. BR = Bendamustine + rituximab. <sup>1</sup>As of May 14, 2018.

# Zanubrutinib Development Program Updates

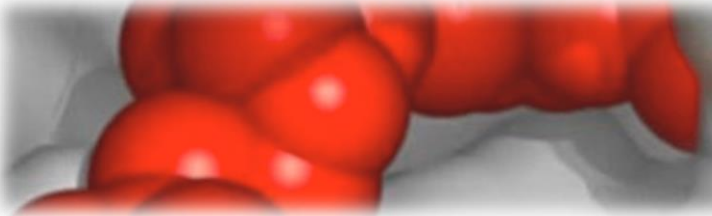
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- Phase III study of zanubrutinib versus ibrutinib in WM: met enrollment target, new patient screening closed, final patient planned to be enrolled in July 2018
  - First US NDA filing for WM expected in 2019
- Independent review of China pivotal Phase II trial in relapsed /refractory MCL (N=86) conducted:
  - Pre-specified primary endpoint met: ORR 84%, CR 59%
  - Safety consistent with previously reported results with zanubrutinib
  - First NDA filing in China for MCL on track for 2018

# Conclusions from EHA Presentations and Development Updates

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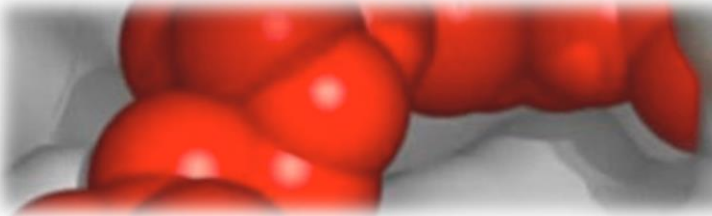
- In total, the data from zanubrutinib studies presented at EHA continue to support our development hypothesis
  - Complete and sustained BTK inhibition can be safely achieved with zanubrutinib
  - Complete and sustained BTK inhibition may be translating into deeper and very durable responses quality
- We anticipate China NDA filings beginning in 2018 and anticipate US NDA filing in Waldenstrom's Macroglobulinemia in 2019
- We are continuing to expand a zanubrutinib clinical trials program aimed at establishing whether zanubrutinib has best-in-class activity and safety in various B cell malignancies



BeiGene

# Q&A

## BeiGene Management



BeiGene

# Appendix



# Overall Response with BTK Inhibitor Treatment in WM\*

WM Efficacy	Zanubrutinib	Acalabrutinib	Ibrutinib	Ibrutinib	Ibrutinib + Rituxan	Placebo + Rituxan
Sources	EHA 2018	ASCO 2018	NEJM 2015	Blood 2017	ASCO 2018	ASCO 2018
Evaluable n	51 12 (TN) 39 (R/R)	106 14 (TN) 92 (R/R)	63 (R/R)	30 (TN)	75 34 (TN) 41 (R/R)	75 34 (TN) 41 (R/R)
mFU	16.9 mo	27.4 mo	19.1 mo <sup>^</sup>	8.1 mo	26.5 mo	26.5 mo
Response Criteria (IWWM)	Modified 6 <sup>th</sup>	Modified 3 <sup>rd</sup>	Modified 3 <sup>rd</sup>	Modified 3 <sup>rd</sup>	Modified 6 <sup>th</sup>	Modified 6 <sup>th</sup>
ORR, n (%)	47 (92%)	99 (93%)	57 (91%)	29 (97%)	69 (92%)	36 (47%)
MRR	41 (80%)	83 (78%)	46 (73%)	24 (80%)	54 (72%)	24 (32%)
<b>VGPR</b>	<b>22 (43%)</b>	<b>31 (29%)</b>	<b>10 (16%)</b>	<b>5 (17%)</b>	<b>17 (23%)</b>	<b>3 (4%)</b>

\*Cross-trial comparisons

<sup>^</sup>Median duration of treatment

Source: Roger, ASCO, 2018; Treon, et al., *NEJM* 2015; Treon, Blood 2017

# Response in WM for Zanubrutinib and Acalabrutinib Assessed by IWWM-6 Criteria\*

	Zanubrutinib			Acalabrutinib		
Source	EHA 2018 Dataset			ASCO 2018		
	TN	R/R	Overall	TN	R/R	Overall
n	12	39	51	14	92	106
mFU	16.9 mo			27.4 mo		
<b>Criteria</b>	<b>IWWM-6</b>					
ORR	12 (100%)	35 (90%)	47 (92%)	13 (93%)	86 (93%)	99 (93%)
MRR	10 (83%)	31 (80%)	41 (80%)	11 (79%)	74 (80%)	85 (80%)
CR	0	0	0	0	0	0
<b>VGPR</b>	<b>3 (25%)</b>	<b>10 (26%)</b>	<b>13 (25%)</b>	<b>0</b>	<b>8 (9%)</b>	<b>8 (8%)</b>
PR	7 (58%)	21 (54%)	28 (54%)	11 (79%)	66 (72%)	77 (73%)
MR	2 (17%)	4 (10%)	6 (12%)	2 (14%)	12 (13%)	14 (13%)

## \*Cross-trial comparisons

MR, minor response; PR, partial response; SD, stable disease; VGPR, very good partial response;

MRR, major response rate; ORR, overall response rate

Source for zanubrutinib: internal data.

# Response in WM for Zanubrutinib and Acalabrutinib Assessed by Modified IWWM-3 Criteria\*

	Zanubrutinib			Acalabrutinib		
Source	EHA 2018 Dataset			ASCO 2018		
	TN	R/R	Overall	TN	R/R	Overall
n	12	39	51	14	92	106
mFU	16.9 mo			27.4 mo		
<b>Criteria</b>	<b>Modified IWWM-3 (IgM only)</b>					
ORR	12 (100%)	35 (90%)	49 (96%)	13 (93%)	86 (93%)	99 (93%)
MRR	10 (83%)	31 (80%)	44 (86%)	11 (79%)	72 (78%)	83 (78%)
CR	0	0	0	0	0	0
<b>VGPR</b>	<b>4 (33%)</b>	<b>18 (46%)</b>	<b>22 (43%)</b>	<b>1 (7%)</b>	<b>30 (33%)</b>	<b>31 (29%)</b>
PR	6 (50%)	13 (33%)	22 (43%)	10 (71%)	42 (46%)	52 (49%)
MR	2 (17%)	4 (10%)	5 (10%)	2 (14%)	14 (15%)	16 (15%)

## \*Cross-trial comparisons

MR, minor response; PR, partial response; SD, stable disease; VGPR, very good partial response;

MRR, major response rate; ORR, overall response rate

Source for zanubrutinib: internal data.

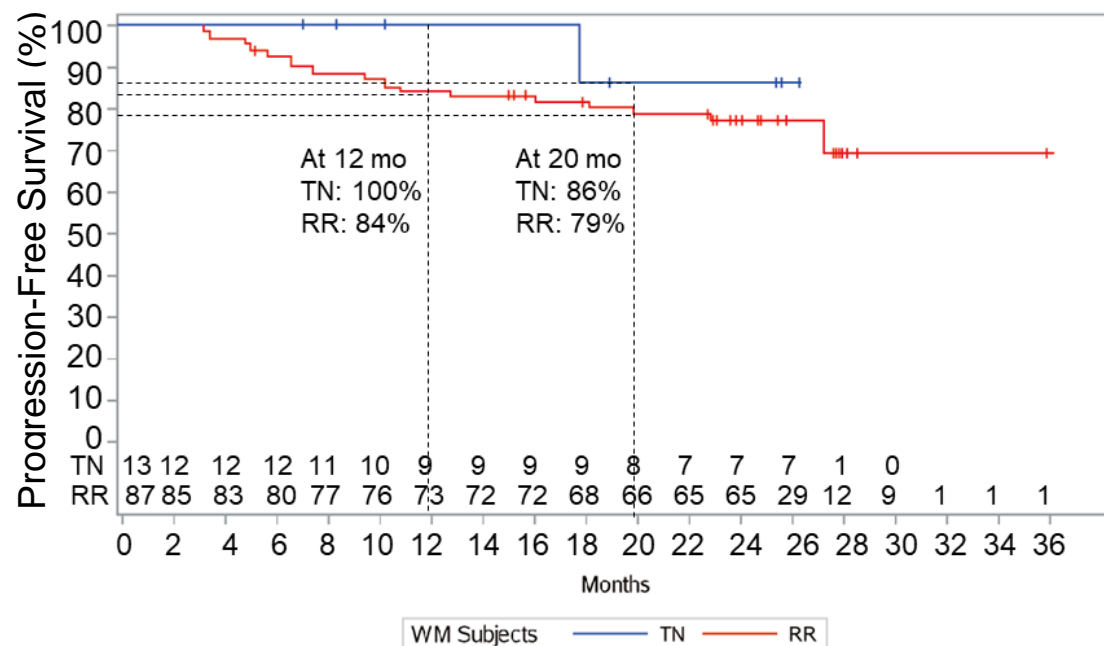
# Response in WM for Zanubrutinib and Ibrutinib Assessed by Modified IWWM-3 Criteria\*

	Zanubrutinib			Ibrutinib
Source	EHA 2018 Dataset			NEJM 2015
	TN	R/R	Overall	R/R
n	12	39	51	63
Criteria	Modified IWWM-3 (IgM only)			
mFU	16.9 mo			19.1 mo**
ORR	12 (100%)	35 (90%)	49 (96%)	57 (90.5%)
MRR	10 (83%)	31 (80%)	44 (86%)	46 (73%)
CR	0	0	0	0
<b>VGPR</b>	<b>4 (33%)</b>	<b>18 (46%)</b>	<b>22 (43%)</b>	<b>10 (16%)</b>
PR	6 (50%)	13 (33%)	22 (43%)	36 (57%)
MR	2 (17%)	4 (10%)	5 (10%)	11 (17%)

\*Cross-trial comparisons

\*\* Duration of treatment of 19.1mo. Source for zanubrutinib: internal data.

# Acalabrutinib in WM: Response Rate and Progression-Free Survival



Acalabrutinib ASCO 2018	TN	R/R	Overall
Criteria	Modified IWWM-3 (IgM only)		
mFU, mos (range)	29.2 (10.2 – 32.9)	27.3 (4.6 – 40.7)	27.4
n	14	92	106
PFS (12 mos)	100%	84%	
PFS (20 mos)	86%	78%	
ORR	13 (93%)	86 (93%)	99 (93%)
MRR	11 (79%)	72 (78%)	83 (78%)
<b>VGPR</b>	<b>1 (7%)</b>	<b>30 (33%)</b>	<b>31 (29%)</b>
PR	10 (71%)	42 (46%)	52 (49%)
MR	2 (14%)	14 (15%)	16 (15%)
SD	1 (7%)	4 (4%)	5 (5%)
Median IgM Reduction (g/L)	0.61 – 7.5 (64%)	0.3 – 9.7 (40%)	
Median Hb Change* (g/dl)	6.2 – 14.1	6.0 – 15.4	

# Adverse Events for Selective BTK Inhibitors\*

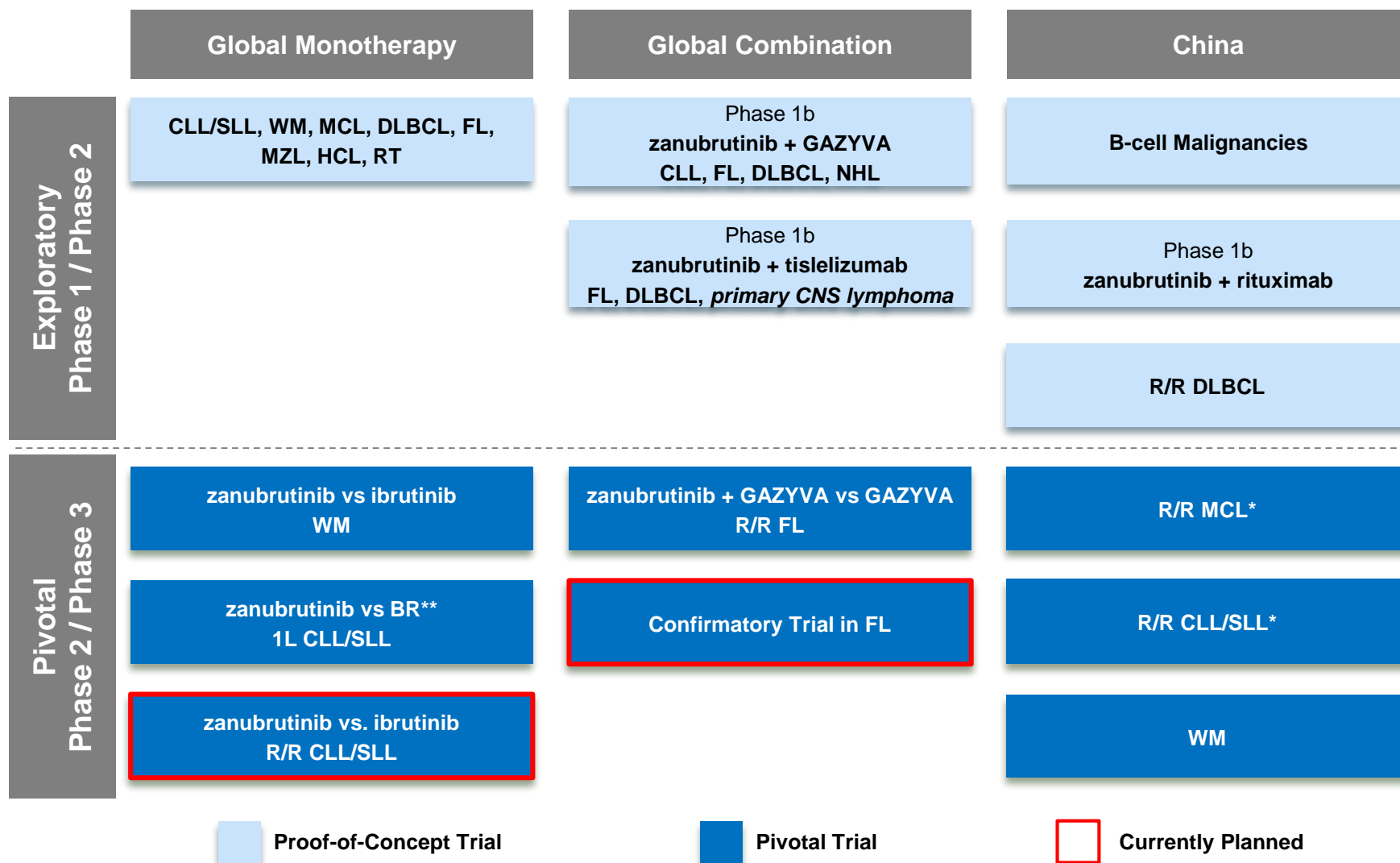
Pooled Safety Data	Zanubrutinib	Acalabrutinib <sup>†</sup>
Source	EHA 2018	ASH 2017
All subject, n	467	612
Duration of exposure (med)	7.0 mo	18.5 mo
Overall AEs, %	94	99
Grade ≥3 AEs, %	42	52
SAEs of Any grade, %	24	39
Treatment-related SAEs, %	8	10
Treatment-related Fatal AEs, %	0.2	0.5
Treatment-related Discontinuation, %	3	6.5
AEs of Interest, %		
Petechiae/purpura/contusion	27	36
Atrial fibrillation/flutter	2	3
Hemorrhage	38	52
Major hemorrhage	2	3
Diarrhea	14	40
Grade ≥3	1	2

\*Cross-trial comparisons

<sup>†</sup>Byrd ASH 2017

# Zanubrutinib Clinical Development Plan

## First NDA Filing in China Expected in 2018



\* R/R MCL completed enrollment in Sept 2017, R/R CLL/SLL completed enrollment in Dec 2017; \*\* BR = bendamustine + rituximab

# Acalabrutinib Response in MCL

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- Acalabrutinib label data:
  - Median follow up: 15.2 months
  - N = 124
  - ORR\*: 80%
  - CR\*: 40%
  - PR\*: 40%

\*Response data as assessed by Independent Review Committee