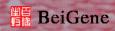


## ASH 2018 Investor Meeting

December 3, 2018



## CFO AND CHIEF STRATEGY OFFICER Dr. Howard Liang



#### Disclosures

- Certain statements contained in this presentation and in the accompanying oral 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 as those regarding continuing and further development and commercialization efforts and transactions with third parties. 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, NMPA (formerly CFDA/CDA) and EMA, the possibility of having to conduct additional clinical trials and BeiGene's reliance on third parties to conduct drug development, manufacturing and other services. 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 (SEC). The reader should not place undue reliance on any forwardlooking statements included in this presentation or in the accompanying oral 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

- Welcome and Introduction, John Oyler, CEO, Dr. Jane Huang, CMO of Hematology, BeiGene
- ASH 2018 Data Reviewed by Professor Yuqin Song:
  - Abstract: 148: Safety and Activity of the Investigational Bruton Tyrosine Kinase Inhibitor Zanubrutinib (BGB-3111) in Patients with Mantle Cell Lymphoma from a Phase 2 Trial
  - Abstract: 1592: Updated Safety and Activity of the Investigational Bruton Tyrosine Kinase Inhibitor Zanubrutinib (BGB-3111) in Patients with Mantle Cell Lymphoma
  - Abstract: 682: Tislelizumab (BGB-A317) for Relapsed/Refractory Classical Hodgkin Lymphoma: Preliminary Efficacy and Safety Results from a Phase 2 Study
- Zanubrutinib and Tislelizumab Development Program, Dr. Eric Hedrick, Chief Advisor, BeiGene
- Q&A with Professor Yuqin Song, Dr. Jane Huang, and Dr. Eric Hedrick



## FOUNDER, CHAIRMAN, AND CEO John V. Oyler



#### **Building a Leading Global Innovative Biotech Company From China**

With the Utmost Commitment to Patients, Quality, and Science



Realize two large near-term commercial opportunities: BTK globally and PD-1 in Asia (ex-Japan)



#### Leverage opportunities created by regulatory reforms in China

- 1.4 billion people reimbursed
- Changes enabling truly global trials



Strengthen unique strategic capabilities - global clinical development and China commercial

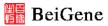


Build global leadership through broad capabilities, robust pipeline, commitment to quality



## Fully-Integrated Biotech Company, Dedicated to Becoming Global Leader 1,700+ People\*

BROAD INTERNAL CAPABILITIES IN CHINA AND GLOBALLY			
Global Clinical Development Team*	Commercial	World-Class Manufacturing Facilities	
<ul> <li>650+ global clinical team</li> <li>300+ China clinical team</li> <li>3,000+ patients and healthy subjects enrolled</li> <li>17 pivotal trials or potentially registration-enabling trials</li> </ul>	China Commercial • Developing top innovative oncology team with 500+ people covering 800+ hospitals Review (enalidomide)	<ul> <li>manufacturing collaborations with: Beehringer Catalent.     </li> <li>Commercial-scale small molecule and pilot biologics manufacturing facility in Suzhou     </li> <li>24,000L biologics facility under construction through strategic collaboration with GDD<sup>(1)</sup> </li> </ul>	
and Globally	Smaller sales team required for hematology than general oncology	MANUFACTURING	
-	registration-enabling trials	registration-enabling trials <b>500+</b> Ongoing or Planned Clinical Trials in China and Globally <b>Clinical Trials</b> in China <b>Clinical Trials</b> in China	



#### Leverage China to Pursue Global Clinical Excellence

BeiGene Is Becoming a Leader in China-Global Clinical Development



Countries where BeiGene is conducting clinical trials account for ~3 billion of the global population

- Pursue a true global model for growth by leveraging China
  - Clinical team of over **650** with **~50%** in China and remainder in US, EU, AU
- Largest oncology-focused clinical development team in China
- Initiated 4 of the first global/China pivotal studies
- **17** pivotal trials or potentially registration-enabling trials
- **50+** ongoing or planned clinical trials in China and globally with **3,000+** subjects enrolled
- Regulatory interactions and monitoring from 20+ countries



#### **Two Late-Stage Assets Represent Significant Commercial Opportunities**

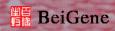
	zanubrutinib Potentially Best-in-Class BTK Inhibitor	<b>tislelizumab</b> PD-1 Inhibitor Targeting Asia-Prevalent Tumors
STRATEGY	Capture significant global market share by demonstrating differentiation	Capture large China opportunity with a broad development program
KEY TARGET INDICATIONS	WM, CLL, MCL (China), FL	Lung, liver, gastric, and esophageal cancers, classical Hodgkin's lymphoma (China), urothelial cancer (China)
FILING PROGRESS	<ul> <li>NDAs for R/R MCL and R/R CLL/SLL accepted by NMPA</li> <li>Priority review status granted to NDA in R/R MCL</li> <li>Fast Track Designation granted by FDA</li> </ul>	<ul> <li>NDA for cHL in China accepted by NMPA</li> <li>Priority review status granted to NDA</li> </ul>
PRELIMINARY FILING DATA IN CHINA*	86-patient R/R MCL <sup>1</sup> 73-patient WM <sup>2</sup> 91-patient R/R CLL/SLL <sup>3</sup> • 84% ORR         • 92% ORR, 82% MRR         • 80% ORR           • 59% CR (8.3mo f/u)         • 41% VGPR (22.5m f/u) • 2% CR (9.1mo f/u)	<ul> <li>70-patient China pivotal Ph2 R/R cHL<sup>4</sup></li> <li>86% ORR</li> <li>61% CR (7.85mo f/u)</li> </ul>
COMMERCIAL	<ul> <li>Establish a global hematology commercial team</li> </ul>	<ul> <li>Leverage growing commercial capabilities in China</li> <li>24,000L biologics manufacturing facility under construction</li> </ul>
CLASS REVENUE & FORECAST**	<ul> <li>2017 Global: \$3.2 billion</li> <li>2025E Global: \$13.8 billion</li> <li>2025E China: \$1.3 billion</li> </ul>	<ul> <li>2017 Global^: \$10.1 billion</li> <li>2025E Global^: \$57.4 billion</li> <li>2025E China^: \$12.1 billion</li> </ul>

1. ASH 2018 Song et al., [Abstract 148]; 2. IWWM 2018 Tam et al.,3. Pivotal trial, BeiGene press release 10/24/18; 4. ASH 2018 Song et al., [Abstract 682]; \*All data are from independent review committee (IRC) assessment. Median follow up time. \*\*Frost & Sullivan analysis; RMB:USD conversion: 6.5:1. ^For PD-1 & PD-L1 class

- 9



# CMO, HEMATOLOGY Dr. Jane Huang



#### Overview of Zanubrutinib (BGB-3111)

Potentially Best-in-Class BTK Inhibitor



**OVERVIEW** 

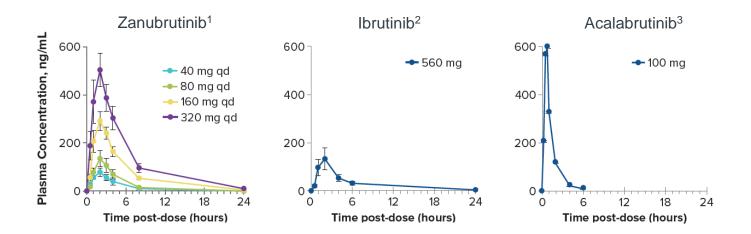
- Bruton's tyrosine kinase (BTK) plays a critical role in B-cell receptor signaling, which mediates B-cell proliferation, migration, and adhesion<sup>1-3</sup>
- Optimized pharmacologic properties relative to ibrutinib: superior bioavailability and higher selectivity
- Development hypothesis: more complete target inhibition, deeper responses, and favorable safety profile
- More than 1,200 patients enrolled across trials, including combinations
- Clinical experience to date supports best-in-class hypothesis
  - Strong suggestion of deeper responses in WM and MCL
  - Favorable response rate, depth, and durability in CLL/SLL
  - High overall and complete response rates in FL with obinutuzumab combination
  - Low rate of toxicity/tolerability-related discontinuation





CLINICAL DATA

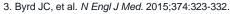
#### Human PK of Zanubrutinib, Ibrutinib, and Acalabrutinib



Note: data are from 3 trials and differences in studies should be considered. 1. Tam CS, et al. *Blood*. 2015;126:832 [oral presentation].

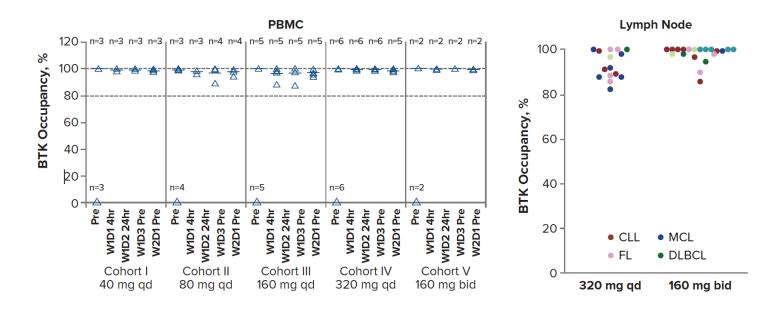
2. Advani RH, et al. *J Clin Oncol.* 2013;31:88-94.

12





#### Sustained BTK Inhibition in Peripheral Blood and Lymph Nodes



- Complete and sustained BTK occupancy is seen in paired PBMC following doses as low as 40 mg (left figure) and lymph node biopsy samples (right figure) collected pre-dose on day 3
- 100% median occupancy at trough plasma concentrations (pre-dose, day 3) at a dose of 160 mg bid; 94% of patients had >90% occupancy in lymph nodes as measured in patients with various B-cell malignancies







#### OVERVIEW

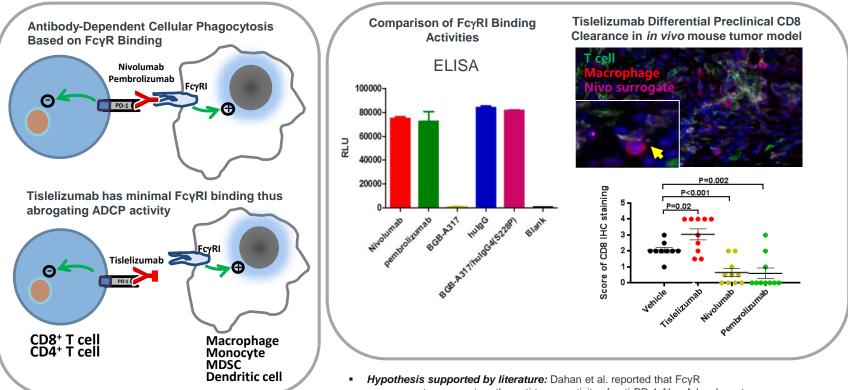
- Tislelizumab is a PD-1 checkpoint inhibitor with distinct molecular structure and an engineered Fc region; believed to minimize potentially negative interactions with other immune cells<sup>1</sup>
- Broad development in Asia-prevalent cancers
  - Including: lung cancer, liver cancer, esophageal cancer, and gastric cancer
  - Also in bladder cancer and Hodgkin's lymphoma
  - Aimed to support broad label and label-based reimbursement
- Strong manufacturing capabilities with emphasis on quality
  - Manufacturing process and initial capacity developed by Boehringer Ingelheim
  - BeiGene's state-of-the-art 24,000L facility in Guangzhou expected to become operational in 2019



 Clinical experience in more than 1,500 patients<sup>2</sup> enrolled over 3 years has demonstrated encouraging clinical activity and generally well-tolerated safety profile



#### Tislelizumab's Lack of FcγR Binding Is Designed to Prevent Macrophage-Mediated T-Cell Clearance



FcγRI=Fc gamma receptor-1, MDSC=myeloid-derived suppressor cell; Source: Dahan et al., Cancer Cell, 2015; Arlauckas et al., Sci. Transl. Med., 2017

15

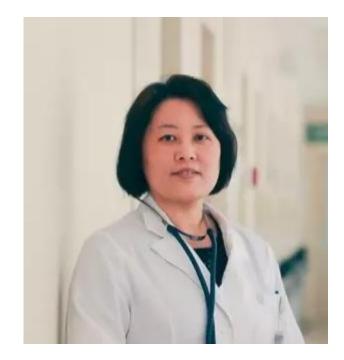
 Hypothesis supported by literature: Dahan et al. reported that FcqR engagement compromises the anti-tumor activity of anti-PD-1 Abs; Arlauckas et al. showed in a mouse model that anti-PD-1 Abs could be transferred from PD-1+ T cells to macrophages in FcqR-dependent manner



### PEKING UNIVERSITY CANCER HOSPITAL, BEIJING, CHINA Professor Yuqin Song, MD, PhD

#### Professor Yuqin Song, MD, PhD

- Associate Professor of Medical Oncology, Deputy Director of the Lymphoma Department of Peking University Cancer Hospital (PUCH)
- Specialist in diagnosis and treatment of lymphoma, focusing on novel therapies
- Leading PI of lymphoma clinical trials at PUCH
- PUCH: 790 beds, 26 departments, 1,100 employees
  - Member of the national base of clinical pharmacology

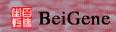




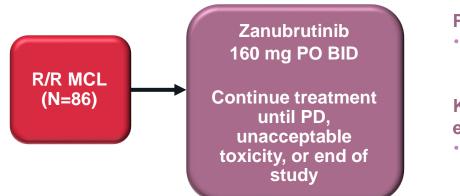
Results of Zanubrutinib Monotherapy in Chinese Patients with Relapsed or Refractory Mantle Cell Lymphoma: A Single Arm, Multicenter, Pivotal Phase 2 Study

<u>YUQIN SONG, MD, PHD</u>,<sup>1</sup> KESHU ZHOU, MD,<sup>2</sup> DEHUI ZOU, MD,<sup>3</sup> JIANFENG ZHOU, PHD,<sup>4</sup> JIANDA HU, PHD,<sup>5</sup> HAIYAN YANG, PHD,<sup>6</sup> HUILAI ZHANG, MD, PHD,<sup>7</sup> JIE JI, MD,<sup>8</sup> WEI XU, MD, PHD,<sup>9</sup> JIE JIN, PHD,<sup>10</sup> FANGFANG LV, MD,<sup>11</sup> RU FENG, MD,<sup>12</sup> SUJUN GAO, PHD,<sup>13</sup> DAOBIN ZHOU, MD,<sup>14</sup> HAIYI GUO, MD,<sup>15</sup> AIHUA WANG, PHD,<sup>15</sup> REBECCA ELSTROM MD,<sup>15</sup> JANE HUANG, MD,<sup>15</sup> WILLIAM NOVOTNY, MD,<sup>15</sup> MUHTAR OSMAN, PHD<sup>15</sup> JUN ZHU, MD<sup>1</sup>

<sup>1</sup>Peking University Cancer Hospital & Institute (Beijing Cancer Hospital), Beijing, China. <sup>2</sup>Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China. <sup>3</sup>Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China. <sup>4</sup>Tongji Hospital, Tongji Medical College, Wuhan, China. <sup>5</sup>Fujian Medical University Union Hospital, Fuzhou, China. <sup>6</sup>Zhejiang Cancer Hospital, Hangzhou, China. <sup>7</sup>Tianjin Medical University Cancer Institute and Hospital, Tianjin, China. <sup>6</sup> West China Hospital of Sichuan University, Chengdu, China. <sup>9</sup>The First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Nanjing, China. <sup>10</sup>The First Affiliated Hospital, Zhejiang University College of Medicine, Hangzhou, China. <sup>11</sup>Fudan University Shanghai Cancer Center, Shanghai, China. <sup>12</sup>Nanfang Hospital of Southern Medical University, Guangzhou, China. <sup>13</sup>The First Hospital of Jilin University, Changchun, China. <sup>14</sup>Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China. <sup>15</sup>BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA, Inc., San Mateo, CA, USA



#### BGB-3111-206: Multicenter, Open-Label, Single-Arm Trial



#### **Primary endpoint:**

 ORR assessed by IRC per the Lugano criteria

Key Secondary endpoints: • PFS, DOR, TTR

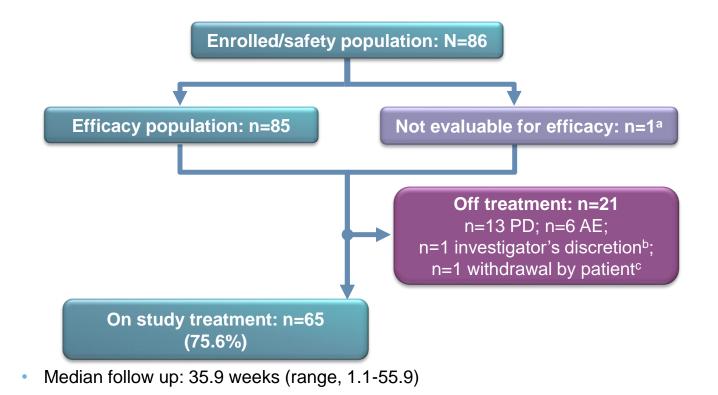
#### **Response assessments:**

 Response assessments were assessed by IRC using PET-based imaging according to the Lugano Classification (Cheson 2014)



#### **Patient Disposition**

20



<sup>a</sup>One subject was excluded due to lack of central pathology confirmation. <sup>b</sup>The subject was discontinued per the investigator's discretion 1 month after starting study drug. <sup>c</sup>The subject achieved CR and withdrew consent.



#### **Patient and Disease Characteristics**

Characteristic	Total (N=86)
Age, years, median (range)	60.5 (34-75)
Sex, n (%) Male Female	67 (77.9) 19 (22.1)
ECOG performance status, n (%) 0/1 2	82 (95.3) 4 (4.7)
Disease status, n (%) Relapse Refractory	41 (47.7) 45 (52.3)
Prior lines of systemic therapy, No., median (range)	2 (1-4)
Stage III/IV disease, n (%)	78 (90.7)
MIPI-b intermediate/high risk, n (%)	72 (83.7)
Bulky disease, n (%) > 10cm > 5cm	7 (8.1) 37 (43)
Blastoid variant of MCL, n (%)	12 (14.0)



#### **Efficacy: Best Overall Response by IRC**

Best response <sup>‡</sup> , n (%)	N=85
ORR (CR or PR), n (%)	71 (83.5)
Complete response	50 (58.8)
Partial response	21 (24.7)
Stable disease	2 (2.4)
Progressive disease	6 (7.1)
Discontinued prior to first assessment <sup>a</sup>	5 (5.9)
No evidence of disease <sup>b</sup>	1 (1.2)

<sup>a</sup> Patients discontinued prior to first disease assessment.

<sup>b</sup>One subject was assessed at Screening by investigator as having one measurable lesion; however, the IRC was unable to identify any measurable disease at baseline.



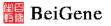
<sup>‡</sup>Response Criteria: Lugano 2014

22

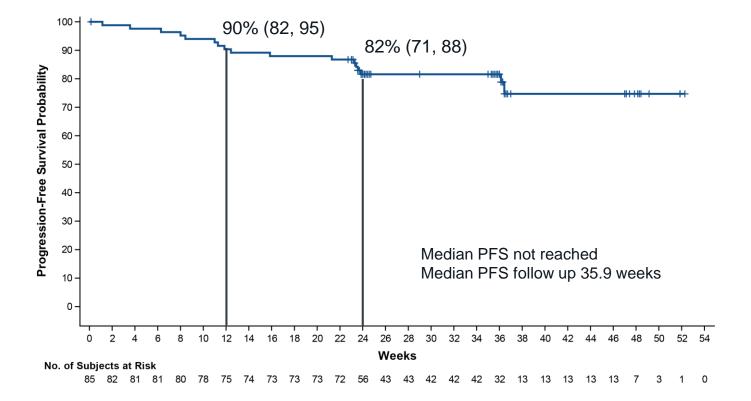
#### Forest Plot of ORR Based on IRC by Subgroup

Subgroup	<b>Response/Subjects</b>	Overall Response Rate (95% CI)	
All patients	71 / 85	<b>_</b>	0.835 (0.739, 0.907)
Sex Male Female	57 / 66 14 / 19	<b>_</b>	0.864 (0.757, 0.936) 0.737 (0.488, 0.909)
Age Group <65 years ≥65 years	58 / 64 13 / 21		0.906 (0.807, 0.965) 0.619 (0.384, 0.819)
Stage at study entry for MCL Stage I or II Stage III Stage IV	5 / 8 13 / 14 53 / 63		0.625 (0.245, 0.915) 0.929 (0.661, 0.998) 0.841 (0.727, 0.921)
ECOG-PS 0 ≥1	51 / 60 20 / 25	<b>•</b>	0.850 (0.734, 0.929) 0.800 (0.593, 0.932)
Prior Line of Therapy for MCL <3 ≥3	49 / 57 22 / 28	<b>_</b>	0.860 (0.742, 0.937) 0.786 (0.590, 0.917)
Blastoid variant form of MCL Yes No Unknown	9 / 12 58 / 67 4 / 6	<b></b>	0.750 (0.428, 0.945) 0.866 (0.760, 0.937) 0.667 (0.223, 0.957)
Ki67-positive cell percentage ≤20% >20%, ≤40% >40%, ≤60% >60% Missing	20 / 23 33 / 40 14 / 16 3 / 5 1 / 1		0.870 (0.664, 0.972) 0.825 (0.672, 0.927) 0.875 (0.617, 0.984) 0.600 (0.147, 0.947) 1.000 (0.025, 1.000)
Bulky Disease Yes (any target lesion LDi >10 cm) No (all target lesion LDi ≤10 cm)	5 / 6 66 / 79		0.833 (0.359, 0.996) 0.835 (0.735, 0.909)
	0.00	0.25 0.50 0.75 1.00	

 Subgroup analysis revealed that the treatment benefit of zanubrutinib was generally consistent across all subgroups analyzed



#### **Progression-Free Survival**





24

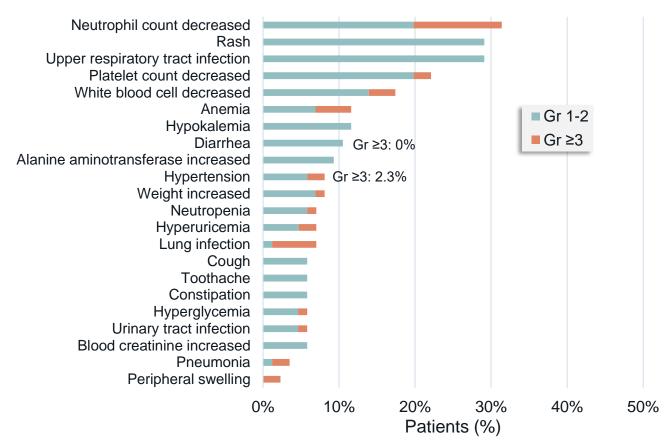
#### Summary of Treatment-Emergent Adverse Events (TEAE) Regardless of Causality

Event, n (%)	N = 86
Grade ≥3 TEAE	28 (32.6)
Serious TEAE	14 (16.3)
TEAE leading to study drug discontinuation	6 (7.0)
TEAE leading to death*	4 (4.7)
TEAE of special interest	
Diarrhea	9 (10.5)
Hypertension	7 (8.1)
Petechiae/purpura/contusion	4 (4.7)
Major hemorrhage <sup>†</sup>	1 (1.2)
Atrial fibrillation/flutter	0

25



#### TEAEs in ≥5% of Patients and Grade ≥3 TEAEs in ≥2 Patients Regardless of Causality





#### Summary

- Zanubrutinib was shown to be highly active in patients with R/R MCL, as demonstrated by:
  - High ORR and CR rate documented by PET-based imaging, (ORR: 84%; CR: 59%)
  - The responses achieved by zanubrutinib treatment appear durable although longer follow-up is needed (median DOR and PFS were not reached)
- Zanubrutinib tolerability was generally consistent with previous reports of zanubrutinib treatment in patients with various B-cell malignancies
- Data from this phase 2 study was included in the NDA submission to Chinese NMPA for zanubrutinib in patients with R/R MCL
- Updated results from a separate ongoing phase 1 study of zanubrutinib in patients with R/R MCL presented as a poster (Tam et al, #1592)



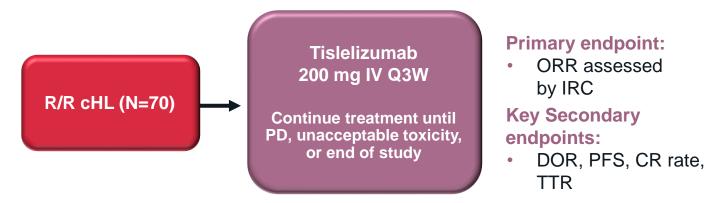
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<sup>1</sup>Key laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Lymphoma, Peking University Cancer Hospital & Institute; <sup>2</sup>Department of Immunotherapy, Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China; <sup>3</sup>Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin, China; <sup>4</sup>Department of Hematology, the First Affiliated Hospital of Nanjing Medical University, Jiangsu Province Hospital, Collaborative Innovation Center for Cancer Personalized Medicine, Nanjing, China; <sup>5</sup>Department of Hematology, Tongji Hospital, Tongji Medical College, Wuhan, China; <sup>6</sup>State Key Laboratory of Experimental Hematology, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; <sup>7</sup>Department of Hematology, Cancer Center, The First Hospital of Jilin University, Changchun, China; <sup>8</sup>Department of Oncology, Zhejiang Cancer Hospital, Hangzhou, China; <sup>9</sup>Department of Hematology, West China Hospital of Sichuan University, Chengdu, China; <sup>10</sup>Department of Hematology, Chinese PLA General Hospital, Beijing, China; <sup>11</sup>Department of Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; <sup>12</sup>Department of Lymphoma and HNC, Fujian Cancer Hospital, Fujian, China; <sup>13</sup>BeiGene (Beijing) Co., Ltd., Beijing, China and BeiGene USA, Inc., San Mateo, CA, USA



#### BGB-A317-203: Multicenter, Open-Label, Single-Arm Trial



#### Patients with R/R HL

Failed to achieve a response or progressed after ASCT

#### or

Received ≥ 2 prior lines of systemic therapy for cHL and was not an ASCT candidate

#### **Response assessments:**

 Response assessments were assessed by IRC using PET-based imaging according to the Lugano Classification (Cheson 2014)



#### **Patient and Disease Characteristics**

Baseline Characteristics	Total (N=70)
Age (years), median (range)	32.5 (18, 69)
Age group <65 / 65-74 years, n (%)	66 (94.3) / 4 (5.7)
Sex, male / female, n (%)	40 (57.1) / 30 (42.9)
Time since first diagnosis of cHL (months), median (range)	25.33 (4.6, 262.3)
Stage IV at study entry, n (%)	42 (60.0)
Bulky disease*, n (%)	8 (11.4)
Bone marrow involvement, n (%)	22 (31.4)
B-symptom(s), n (%)	26 (37.1)
Ineligible for prior ASCT <sup>+</sup> , n (%)	
Failure to achieve an objective response to salvage chemotherapy	53 (75.7)
Inadequate stem cell collection or unable to collect stem cells	2 (2.9)
Co-morbidities	2 (2.9)
Prior lines of systemic therapy, median (range)	3 (2-11)
Type of prior therapy, n (%)	
Chemotherapy	70 (100.0)
Radiotherapy	21 (30.0)
ASCT	13 (18.6)
Immunotherapy <sup>‡</sup>	15 (21.4)
Brentuximab vedotin	4 (5.7)

\*Mediastinal mass ratio of 0.33 or size of any single node/nodal mass ≥10 cm in diameter.

<sup>†</sup>All received  $\geq$  2 prior regimens.

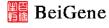
30

<sup>‡</sup>Immunotherapy included brentuximab vedotin, rituximab, cytokine-induced killer cell transfusion, thalidomide, and lenalidomide.



#### **Efficacy: Best Overall Response by IRC**

Best response*, n (%)	N=70
ORR (CR+PR), n (%) [95% CI] <sup>†</sup>	60 (85.7) [75.3,92.9]
Complete response	43 (61.4)
Partial response	17 (24.3)
Stable disease	4 (5.7)
Progressive disease	5 (7.1)
Died before any postbaseline tumor assessment <sup>‡</sup>	1 (1.4)

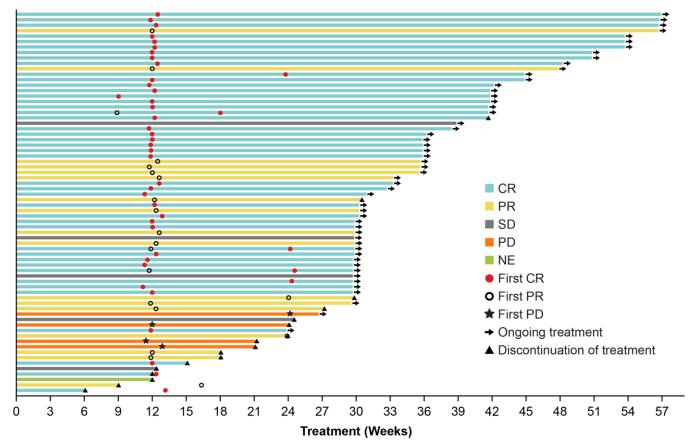


#### Forest Plot of ORR Based on IRC by Subgroup

Subgroup	<b>Response/Patients</b>		ORR,% (95% CI)*
All patients	60/70	<b></b>	85.7 (75.3, 92.9)
Age group			
Age < 65	57/66	<b>_</b> _	86.4 (75.7, 93.6)
Age ≥ 65	3/4		75.0 (19.4, 99.4)
Sex			
Male	33/40	<b>_</b>	82.5 (67.2, 92.7)
Female	27/30	<b>_</b>	90.0 (73.5, 97.9)
Primary refractory			
Yes	20/25	•	80.0 (59.3, 93.2)
No	40/45	<b>_</b>	88.9 (75.9, 96.3)
Prior line of therapy for cHL			
< 3	25/28	•	89.3 (71.8, 97.7)
≥ 3	35/42	<b>_</b>	83.3 (68.6, 93.0)
Bulky disease			
Yes	6/8	•	75.0 (34.9, 96.8)
No	54/62	<b>_</b>	87.1 (76.1, 94.3)
Prior ASCT			
Yes	12/13	•	92.3 (64.0, 99.8)
No	48/57	<b>_</b>	84.2 (72.1, 92.5)
Prior Brentuximab			
Yes	4/4	•	100.0 (39.8, 100.0)
No	56/66	<b>_</b>	84.8 (73.9, 92.5)
	0	10 20 30 40 50 60 70 80 90 100	
		Patients with an objective response (%)	

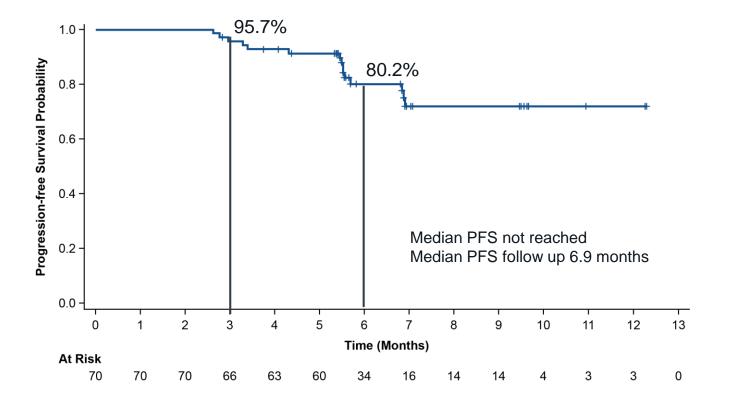
Patients with an objective response (%)

#### **Duration of Treatment and Time to Response**





#### **Progression-Free Survival**



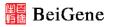


#### **Summary of Treatment-Emergent Adverse Events**

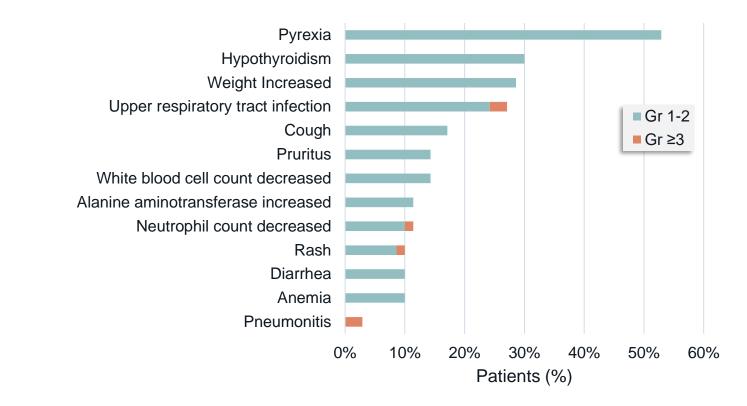
Event, n (%)	N=70
Grade ≥3 TEAE	15 (21.4)
Serious TEAE <sup>1</sup>	11* (15.7)
TEAE leading to treatment discontinuation	4† (5.7)
TEAE leading to death	0 (0.0)
Immune-related (ir) TEAEs (by aggregate category)	
≥1 irTEAE	24 (34.3)
Thyroid disorder	13 (18.6)
Pneumonitis	4 (5.7)
Skin adverse reactions	4 (5.7)
Musculoskeletal <sup>‡</sup>	2 (2.9)
Hepatitis	1 (1.4)
Nephritis and renal dysfunction	1 (1.4)

\*SAEs in all 11 patients determined to be possibly related to tislelizumab. <sup>†</sup>Pneumonitis (n=2), focal segmental glomerulosclerosis (n=1), organizing pneumonia (n=1) <sup>‡</sup>Blood creatine phosphokinase increased, osteoarthritis

35



#### TEAEs in ≥10% of Patients and Grade ≥3 TEAEs in ≥2 Patients Regardless of Causality





## Summary

- Tislelizumab is an investigational anti-PD-1 mAb specifically designed to minimize binding to FcγR on macrophages
- Tislelizumab was generally well-tolerated, and the safety profile was similar to that of other anti-PD1 antibodies for the treatment of cHL
- Tislelizumab was shown to be highly active in patients with R/R cHL who failed or were ineligible for ASCT, as demonstrated by:
  - High ORR and rate of CR (86% and 61%, respectively)
  - Median duration of response not reached

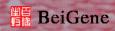


#### **Acknowledgements**

- We would like to thank the investigators, site support staff and especially the patients for participating in this study
- This study was sponsored by BeiGene; editorial support was provided by Bio Connections LLC and funded by BeiGene



## CHIEF ADVISOR Dr. Eric Hedrick



#### **Tislelizumab: Clinical Development Summary**

- Solid tumor indications (joint development with Celgene)
  - Seven global (China and rest-of-world inclusive) Phase 3 or potentially registration-enabling trials ongoing or to initiate in the near term
    - Hepatocellular Cancer: Phase 2 2L/3L trial, 1L Phase 3 tislelizumab vs sorafenib
    - Gastric Cancer: 1L chemotherapy +/- tislelizumab
    - Esophageal cancer (squamous): 2L Phase 3 tislelizumab vs chemotherapy, 1L Phase 3 chemotherapy +/tislelizumab
    - Non-small cell lung cancer: 2L Phase 3 tislelizumab vs chemotherapy, Phase 3 locally advanced NSCLC (tislelzumab in combination with radiation)
  - Three ongoing pivotal trials in China:
    - Non-small cell lung cancer: 1L Phase 3 in squamous histology
    - Non-small cell lung cancer: 1L Phase 3 in non-squamous histology
    - Bladder cancer: pivotal Phase 2
- Hematologic malignancy indications (BeiGene retains global rights)
  - Hodgkin Lymphoma
    - NDA filed in China based on Pivotal Phase 2 study under priority review
    - Global development strategy in discussion
  - NK/T cell lymphomas: global Phase 2 trial is enrolling



## **Reported PD-1 Inhibitor Data in R/R cHL\***

Evaluated in patients who had failed brentuximab vedotin and/or ASCT

	Opdivo <sup>2</sup>							
Ν	2	258						
Prior Lines (med)	4 (1	4 (1-12)						
Follow-up (med)	15.9	15.9 mo						
Response Criteria	Cheson 2007	Cheson 2007						
ORR	71%	<b>73</b> %ª	69%					
CR	25%	31% <sup>b</sup>	14%					
PR	47%	42%	55%					
SD	12%	-						

<sup>a</sup> 2-yr follow-up for response durability (Zinzani, ASH 2018): med DOR 11.1 mo (ASCT-ineligible) vs 22.1 mo (ASCT failure followed by BV) vs 24.4 mo (ASCT failure)

<sup>b</sup> 2-yr follow-up for response durability (Zinzani, ASH 2018): med DOR NR (CR pts) vs 10.9 mo (PR pts)

41



## Reported PD-1 Inhibitor Data in R/R cHL (China Studies)\*

#### Patient population: Primarily ASCT-ineligible

	sintilimab <sup>1</sup>	camrelizumab <sup>2</sup>
Company	Innovent	Hengrui
Ν	96	66
Prior Lines (med)	3 (1-13)	3 (2-10)
Follow-up (med)	>6 months	>6 months
Response Criteria	Cheson 2007	Lugano 2014
ORR	79%	85%
CR	18%	30%
PR	62%	54%
SD	19%	12%

42



#### **Tislelizumab in Refractory cHL**

Ν	70
Prior Lines of therapy (median; range)	3 (2-11)
Follow-up (median)	7 months
Response Criteria	Lugano 2014
ORR	86%
CR	61%
PR	24%
SD	6%
PD or d/c prior to first assessment	9%



### Zanubrutinib: Clinical Development Summary

- Single-arm data continues to support potential clinical benefits of sustained BTK occupancy and high BTK selectivity:
  - Depth of response:
    - Favorable VGPR rate in Phase 1 WM trial (77 patients enrolled)
    - Majority of MCL patients in pivotal Phase 2 MCL trial achieved CR
  - Low rates of toxicity-related treatment discontinuation and off-target tolerability issues
- China NDA filings for CLL and MCL (MCL under priority review)
- Phase 3 trial to support rest-of-world filing in WM has completed enrollment
- Global registrational program has expanded to seek at least 5 additional indications
- Development program objectives:
  - Pursuit of global (China, US, EU) registration in multiple B cell malignancies
  - Evaluation of potential clinical distinctions between zanubrutinib and ibrutinib
    - Focus on aspects compatible with sustained therapy



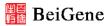
#### Zanubrutinib Clinical Development Status December 2017

			Lead Indications			
China	Phase 2 Pivotal R/R CLL/SLL	*	Phase 2 Pivotal R/R MCL	*	Phase 2 Pivotal R/R WM	
ROW	Zanubrutinib vs. Ibrutinib WM	<b>@</b>	Phase 1 WM	9		
		Additiona	al Global Registrational Pro	grams		
CLL	Phase 3 Zanubrutinib vs. BR 1L CLL/SLL					
FL	Phase 2 Pivotal Obinutuzumab ± Zanubrutinib R/R FL	<b>@</b>				
		Addition	al Indications and Combina	ations		
DLBCL	Phase 2: Monotherapy, R/R Non- Phase 1b Zanubrutinib + tisle		CLL Combination	Pha	ase 1b: Zanubrutinib + obinutuzumab, R/R CLL	

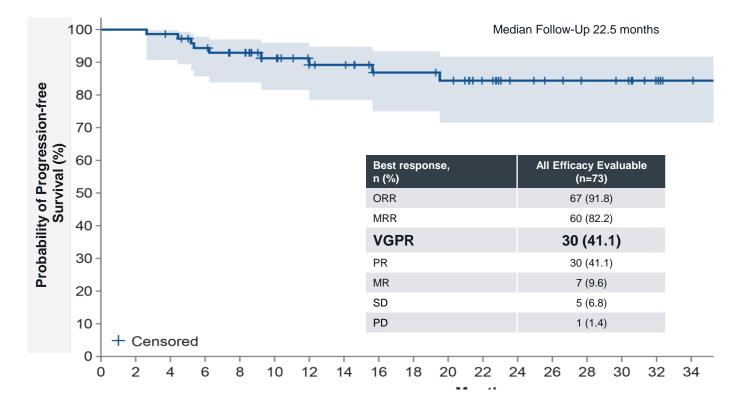


#### Zanubrutinib Clinical Development Status December 2018

		Lead Indications			Enrolling
China	Phase 2 Pivotal <b>*</b> R/R CLL/SLL	Phase 2 Piv R/R MCL		Phase 2 Pivotal R/R WM	Enrollment Complete
ROW	Zanubrutinib vs. Ibrutinib 🕥 WM	Phase 1 WM	<b>@</b>		Planned
	Additio	nal Global Registration	al Programs		Filed, In NDA review
CLL	Phase 3 Zanubrutinib vs. BR S 1L CLL/SLL	Phase Zanubrutinib v R/R CLL	s. Ibrutinib 🌍		In discussion with FDA
FL	Phase 2 Pivotal Obinutuzumab ± Zanubrutinib R/R FL				
MCL	Phase 3 R+zanu vs. R+chemo 1L MCL				
MZL	Phase 2 Pivotal Zanubrutinib monotherapy R/R MZL				
	Additic	onal Indications and Co	ombinations		
DLBCL	Phase 2: Monotherapy, R/R Non-GCB DLBCL Phase 1b/2: Zanubrutinib + tislelizumab, PCNSL and	RT CLL	Phase 1b: Zanub	orutinib + obinutuzumab, R/R CLL	
	Phase 1b: Zanubrutinib + revlimid, R/R DLBCL Phase 1b: Zanubrutinib + R-chemo, 1L and 2L DLBC	Combination	Phase 2: Bendamustine	/ venetoclax/ obinutuzumab in 1L CLL e followed by Zanubrutinib / venetoclax/ utuzumab in 1L CLL	

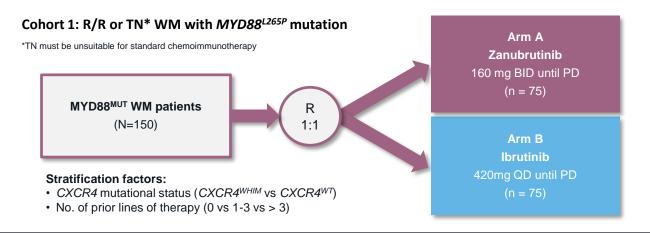


#### Zanubrutinib in WM





#### Phase 3 Study: Zanubrutinib vs. Ibrutinib in WM

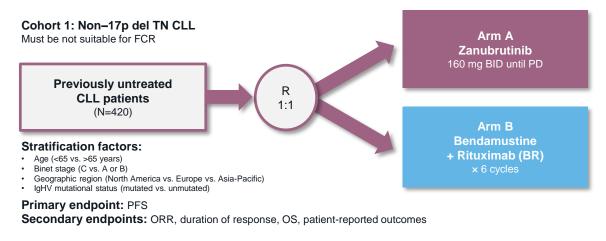


#### Cohort 2: WM with wild type MYD88; present in ~10% of enrolled patients





#### Phase 3 Study of Zanubrutinib vs. BR in 1L CLL/SLL

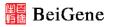


Cohort 2: 17p del TN CLL

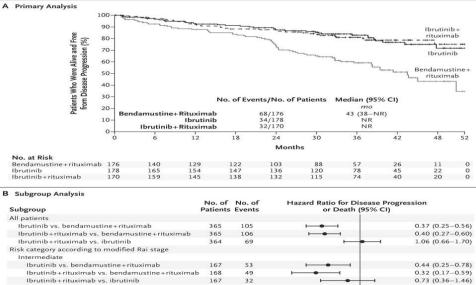
49



1L=first-line treatment for CLL/SLL; BID=twice daily, CLL=chronic lymphocytic leukemia, FCR=fludarabine, cyclophosphamide, and rituximab, ORR=overall response rate, OS=overall survival, PD=progressive disease, PFS=progression-free survival, R=randomization, SLL=small lymphocytic lymphoma, TN=treatment naive This study is registered at ClinicalTrials.gov (NCT0336333).



#### Single-Agent Ibrutinib Significantly Prolongs PFS Compared to Bendamustine/ Rituximab



All patients					
Ibrutinib vs. bendamustine+rituximab	365	105	H		0.37 (0.25-0.56)
Ibrutinib+rituximab vs. bendamustine+rituximab	365	106	<b>⊢</b> •−−1		0.40 (0.27-0.60)
Ibrutinib+rituximab vs. ibrutinib	364	69			1.06 (0.66-1.70)
Risk category according to modified Rai stage					
Intermediate					
Ibrutinib vs. bendamustine+rituximab	167	53			0.44 (0.25-0.78)
Ibrutinib+rituximab vs. bendamustine+rituximab	168	49			0.32 (0.17-0.59)
Ibrutinib+rituximab vs. ibrutinib	167	32			0.73 (0.36-1.46)
High					
Ibrutinib vs. bendamustine+rituximab	198	52			0.33 (0.18-0.60)
Ibrutinib+rituximab vs. bendamustine+rituximab	197	57	· • • • • •		0.50 (0.29-0.85)
Ibrutinib+rituximab vs. ibrutinib	197	37			1.44 (0.75-2.76)
Status with regard to del(17p13.1) or del(11q22.3)					
Absent					
Ibrutinib vs. bendamustine+rituximab	263	70			0.44 (0.27-0.72)
Ibrutinib+rituximab vs. bendamustine+rituximab	265	72			0.50 (0.31-0.80)
Ibrutinib+rituximab vs. ibrutinib	266	52		• •	1.11 (0.65-1.92)
Present					
Ibrutinib vs. bendamustine+rituximab	102	35			0.26 (0.12-0.56)
Ibrutinib+rituximab vs. bendamustine+rituximab	100	34			0.24 (0.11-0.53)
Ibrutinib+rituximab vs. ibrutinib	98	17	F		0.90 (0.35-2.32)
ZAP70 methylation status					
Unmethylated					
Ibrutinib vs. bendamustine+rituximab	191	61			0.19 (0.11-0.35)
Ibrutinib+rituximab vs. bendamustine+rituximab	191	68			0.31 (0.18-0.51)
Ibrutinib+rituximab vs. ibrutinib	192	35	H		1.57 (0.80-3.09)
Methylated					
Ibrutinib vs. bendamustine+rituximab	173	43			0.81 (0.45-1.48)
Ibrutinib+rituximab vs. bendamustine+rituximab	173	37		-	0.58 (0.30-1.12)
Ibrutinib+rituximab vs. ibrutinib	172	34			0.72 (0.36-1.43)
		0.062	0.1250 0.2500 0.5000 1.0	00 2.000 4	.000
		-	Better	Worse	-



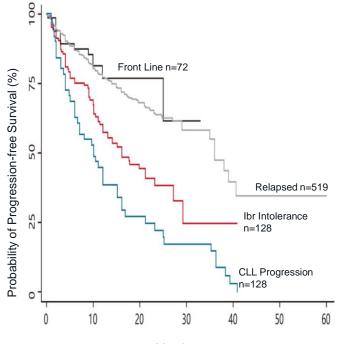
#### **Tolerability Issues With Long-Term Ibrutinib Use in CLL**

Single-agent BTKi treatment in CLL requires prolonged use:

Discontinuation for all reasons compromises PFS<sup>3</sup>

Tolerability or toxicity concerns with long-term ibrutinib use:

- Musculoskeletal events (myalgia/ arthralgia)<sup>1</sup>
  - 38% cumulative incidence
  - Mean time to onset: 349 days
- Hypertension<sup>2</sup>
  - 70% new onset, 84% worsening in patients with pre-existing HTN
- Overall toxicity/ tolerability-related treatment discontinuation
  - AE-related discontinuation reported as high as 22% within first 2 years of therapy<sup>3</sup>



Months

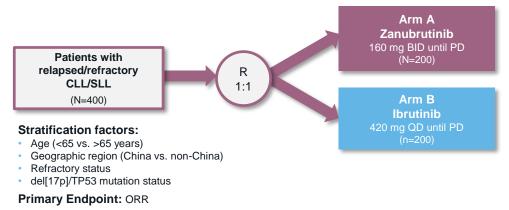


#### Phase 3 Study of Zanubrutinib vs. Ibrutinib in R/R CLL/SLL

**R/R CLL/SLL** 

52

- Refractory no objective response to or disease progression within 6 months after last treatment
- Relapsed <6 months from end of last treatment and subsequently progressed



**Secondary Endpoints:** PFS, duration of response, OS, patient-reported outcomes



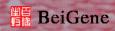
#### **Key Upcoming Milestones**

- Approval and launch of zanubrutinib in China in 2019
  - Zanubrutinib MCL and CLL
  - Tislelizumab cHL
- Phase 3 zanubrutinib vs. ibrutinib data in WM anticipated in 2H 2019
- NDA filing for zanubrutinib in WM in the US in 2019 or early 2020





# Supporting Information



#### BeiGene Presentations at ASH 2018



- Oral Presentation: Safety and Activity of the Investigational Bruton Tyrosine Kinase Inhibitor Zanubrutinib (BGB-3111) in Patients with Mantle Cell Lymphoma from a Phase 2 Trial Publication Number: 148 Saturday, December 1, 2018
- Poster: Updated Safety and Activity of the Investigational Bruton Tyrosine Kinase Inhibitor Zanubrutinib (BGB-3111) in Patients with Mantle Cell Lymphoma Publication Number: 1592 Saturday, December 1, 2018
- Oral Presentation: Tislelizumab (BGB-A317) for Relapsed/Refractory Classical Hodgkin Lymphoma: Preliminary Efficacy and Safety Results from a Phase 2 Study Publication Number: 682 Monday, December 3, 2018



#### **2018 Accomplishments** MAY

CCC CCC CCCC 500+ in clinical dev 500+ in commercia	,	President	er of China and		JUL Fast track FDA for W		ignation by	~	Appointed Jonat SVP, Bio-Manuf	han			ост
() () () () () () () () () () () () () (	anization Market Access		$\checkmark$			√	Appointed Diana Global Head, Qu GxP Compliance	uality and		~	Zanubrutinib China NDA R/R CLL/SLL acceptance by NMPA		
since Jan 20	•	trial in China in V	Ilment in Ph2 pivotal WM P3 trial of pamiparib		70-patient Ph2 in R/R flw up)			✓ ●	Presented tisleli Chinese NSCLC WCLC			✓ )	Topline China pivotal Ph2 in CLL/SLL (9.1 mo follow up)
product rev ✓ VIDAZA cc	irst full quarter venues of \$15.6M ommercial launch	as maintenance	therapy in OC product revenues of	1	• 73% Initiated Ch tislelizumat	ina		~	Presented tisleli MSI-high solid tu Chinese lung ca	umo	ors and	✓	• 80% ORR Presented zanubrutinib in WM global Ph1 data
	approval for nosed multiple n China	in Jiangsu	lusion in the PRDL n Basel, Switzerland	~	NSCLC Initiated glo	bal		~	CSCO Presented zanul Chinese B-cell ly CSCO				at IWWM • 82% MRR, 41% VGPR
<ul> <li>JAN</li> <li>✓ Commercial supply agreement with Boehringer Ingelheim for tislelizumab</li> <li>✓ Exclusive license agreement with Mirati Therapeutics for sitravatinib in APAC</li> <li>✓ Closed \$800 million public offering</li> <li>✓ Initiated global Ph3 trials of</li> </ul>	<ul> <li>APR</li> <li>Appointed Yifei Z Chief Commercia Sales and Market</li> <li>✓ Initiated global P tislelizumab in 2l</li> <li>✓ Initiated global P tislelizumab in r/r lymphoma</li> <li>✓ Presented data of</li> </ul>	Zhu as Co al Officer, et Access Ph2 trial of L/3L HCC P2 trial of r NK/T-cell on pamiparib in	in WM and pooled s EHA	from fib (	ty data at n 476 (2%, only e	✓ ✓ ✓	AUG Successful Hł on HKEx; \$90 Zanubrutinib MCL accepta Tislelizumab acceptance k • 86% Of Initiated China tislelizumab in	OM Chi nce Chi by N RR, a Ph	ina NDA R/R by NMPA ina NDA cHL MPA 61% CR 3 trial of	<ul> <li>○</li> <li>✓</li> <li>✓</li> <li>✓</li> </ul>	VIDAZA Presente pamipar at ESMC Clinical Pharma Launche	ed rib+ O coll in ed I	Clusion in NRDL preliminary data on -TMZ in solid tumors laboration with MEI B-cell malignancies REVLIMID Patient Program (PAP)
tislelizumab in HCC and ESCC ✓ ABRAXANE inclusion in critical 57 <sup>illness</sup> insurance in Zhejiang	Chinese TNBC p AACR	oatients at	<ul> <li>86-patient China p R/R MCL (8.3mo fo</li> <li>84% ORR, 599</li> </ul>	ollov	w up)	✓ ✓	of \$31.4M, 35 Commenced I	% c KUE	roduct revenues QoQ growth Bio installation in Ifacturing facility				BeiGene

SEP

✓ Global clinical collaboration with SpringWorks