BeiGene

2022 ASH Data

DECEMBER 11, 2022

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 statements regarding BeiGene's research, discovery, and pre-clinical and early-stage clinical programs and plans; recent clinical data for BeiGene's product candidates and approvals of its medicines; the conduct of late-stage clinical trials and expected data readouts; additional planned commercial product launches; and the advancement of and anticipated clinical development, regulatory milestones and commercialization of BeiGene's medicines and drug candidates. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including BeiGene's ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; BeiGene's ability to achieve commercial success for its marketed medicines and drug candidates, if approved; BeiGene's ability to obtain and maintain protection of intellectual property for its technology and medicines; BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited experience in obtaining regulatory approvals and commercializing pharmaceutical products and its ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates and achieve and maintain profitability; the impact of the COVID-19 pandemic on BeiGene's clinical development, commercial, regulatory and other operations, as well as those risks more fully discussed in the section entitled "Risk Factors" in BeiGene's most recent periodic report filed with the SEC, as well as discussions of potential risks, uncertainties, and other important factors in BeiGene's subsequent filings with the SEC. All information in this presentation is as of the date of this presentation, and BeiGene undertakes no duty to update such information unless required by law.

Some of the clinical data in this presentation relating to BeiGene's investigational drug candidates is from pre-clinical studies or early phase, single-arm clinical trials. When such data or data from later stage trials 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 unless specified in the trial protocol. BeiGene is still conducting pre-clinical studies and 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 contain 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 & SPEAKERS

- **Welcome:** John V. Oyler
- **R&D Evolution & BRUKINSA® Introduction:** Lai Wang, Ph.D.
- **BRUKINSA® Clinical Overview & ALPINE:** Mehrdad Mobasher, M.D., M.P.H.
- **BRUKINSA® Data:** Mazyar Shadman, M.D., M.P.H.
- **BGB-11417 (BCL2i) Introduction:** Dr. Mobasher
- **BGB-11417 (BCL2i) Data:** Constantine S. Tam, M.B.B.S., M.D.
- **BGB-16673 (BTK-CDAC):** Dr. Mobasher
- **Key Takeaways:** John V. Oyler
- **Q&A Panel:** Dr. Mobasher, Moderator

BeiGene

Welcome

John V. Oyler
Co-Founder, Chairman, and CEO

CANCER HAS NO BORDERS. NEITHER DO WE.

Our vision is to create impactful medicines that will be affordable and accessible to far more cancer patients around the world.

BeiGene: Unique Among Global Biotech Companies

Global 9,000+ organization • Broad portfolio of ~50 clinical/commercial assets • Clinical trials in 45+ geographies

RESEARCH

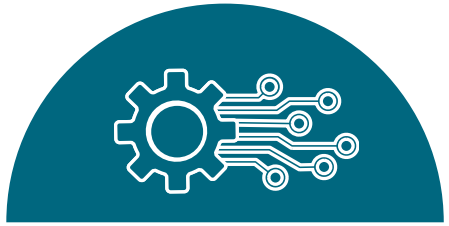
- One of the world's largest oncology teams (900+)
- 60+ pre-clinical programs, the majority with first-in-class potential
- Passionate, entrepreneurial, science-based culture
- Burst of new clinical molecules expected in the next few years, 10+ INDs per year expected starting from 2024

DEVELOPMENT

- 2,300+ internal clinical development colleagues
- Experience running 15 global Phase 3 oncology trials
- Predominantly CRO free
- More inclusive development (e.g., Australia, China, Poland) enabling cost and time savings
- ~50 assets in clinical and commercialization stages
- 20,000+ subjects enrolled
- 110+ clinical trials initiated since 2013, 35 filed or potentially registration-enabling trials ongoing

COMMERCIAL

- ~3,200 in China, competitively positioned, science-based leadership with 16 commercial products, leading market share in PD-1 and BTK classes
- 300+ competitive footprint in North America and Europe
- Expanding presence in multiple countries/regions, including underserved areas



MANUFACTURING

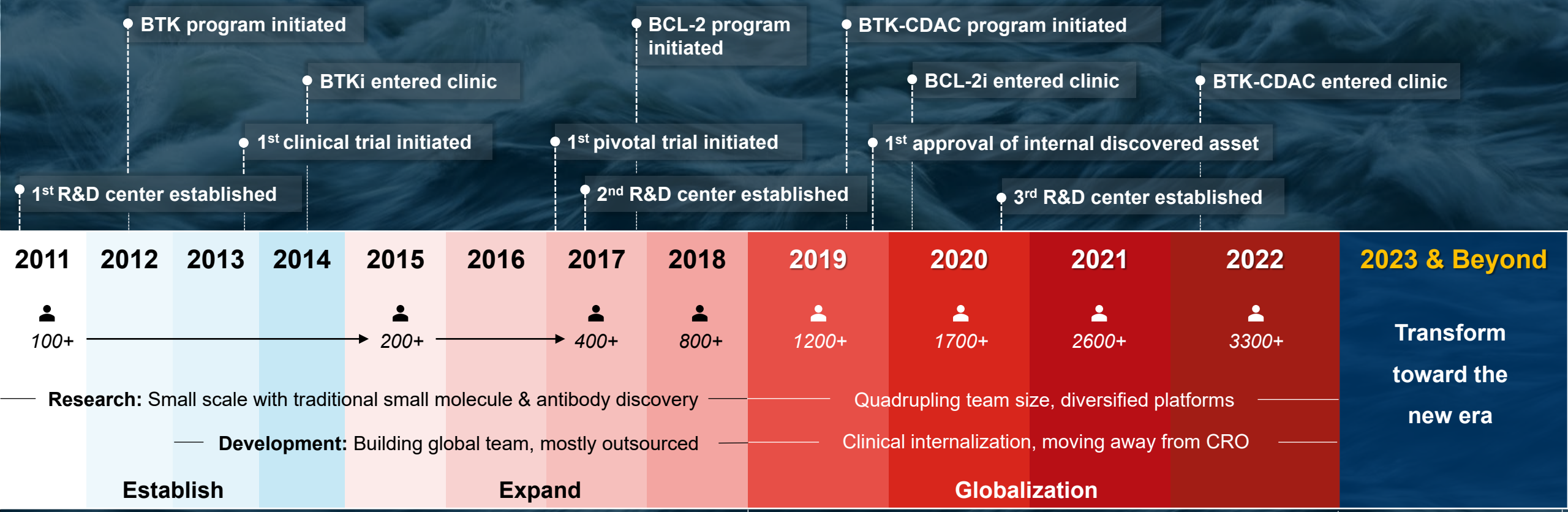
- In-house capabilities reduce cost and provide agility/flexibility
- State-of-the-art standards and technologies
- Expanding biologics capacity up to 200,000L
- Construction underway on 42-acre biologics site at Princeton Innovation Center in New Jersey

CRO: contract research organization

R&D Evolution and BRUKINSA® Introduction

Lai Wang, Ph.D.
Global Head of R&D

BeiGene R&D Evolution



End of 2018

- 6 internally discovered molecules to the clinic
- 10 commercial and clinical pipeline
- 9 pre-clinical programs

Today

- 16 internally discovered molecules to the clinic
- ~50 commercial and clinical pipeline
- 60+ pre-clinical programs

Starting from 2024

- 10+ NME into clinic per year

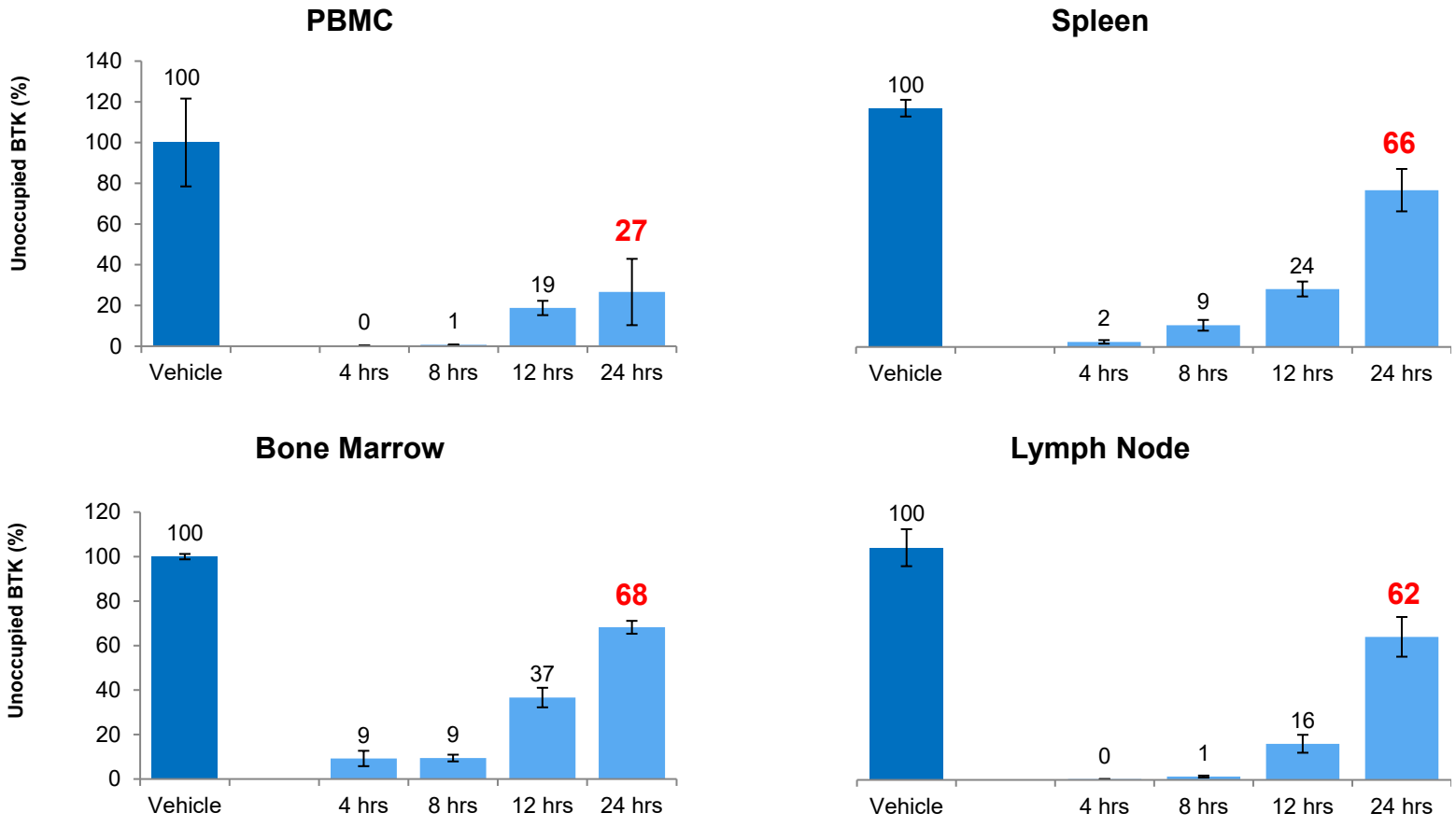
CDAC: Chimeric Degradation Activating Compound; NME: New Molecule Entity

BeiGene

The Journey of BRUKINSA®

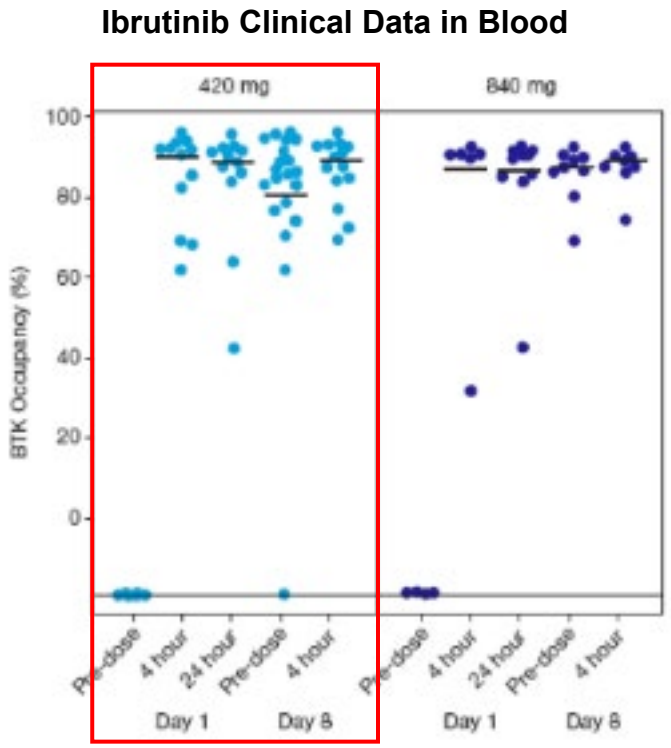
The Journey Started with the BTK Occupancy Issue Associated with Ibrutinib

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



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

Borderline BTK occupancy by ibrutinib in the blood in clinic



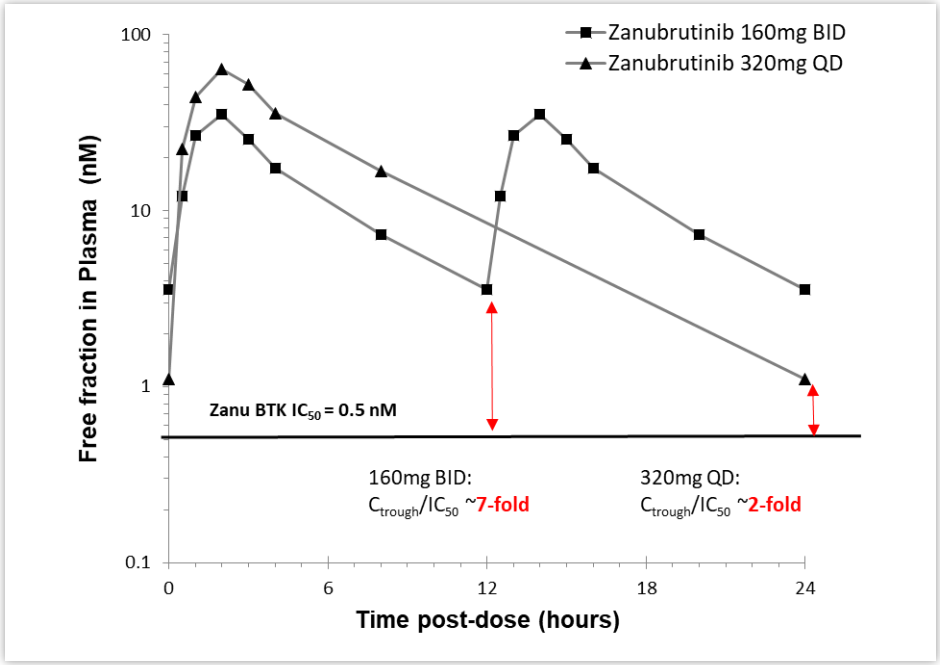
Approved Ibrutinib Doses:
420 mg for CLL and WM; 560 mg for MCL

Byrd *et al.*, NEJM, 2013

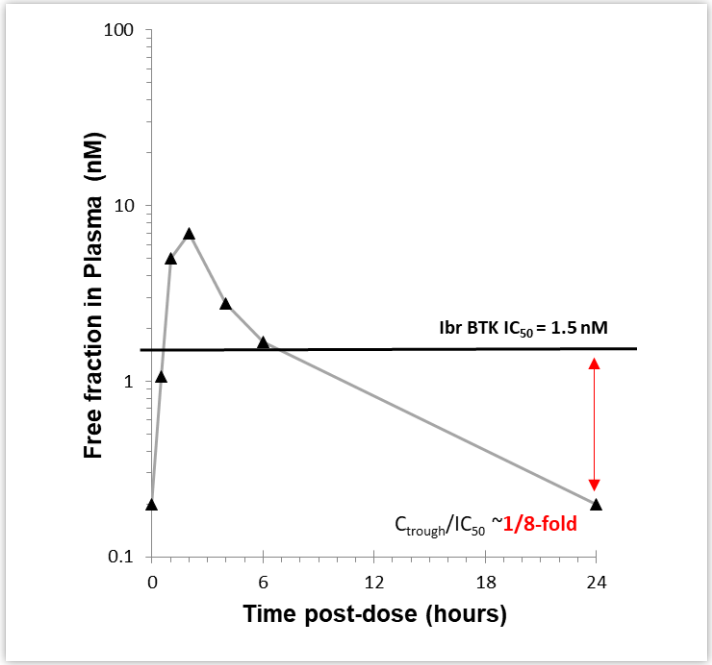
Favorable Zanubrutinib Pharmacokinetic Profile Compared to Acalabrutinib and Ibrutinib

Free Drug Concentration Time Profiles Relative to IC_{50}

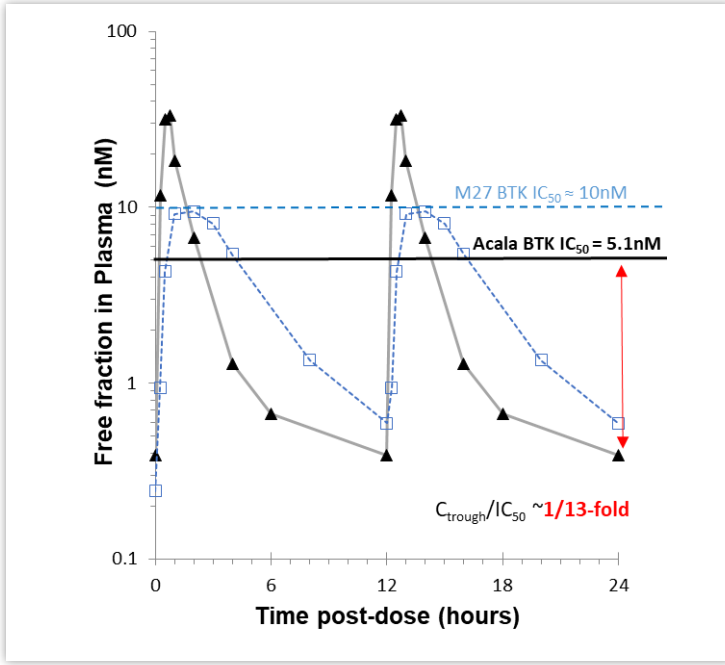
Zanubrutinib



Ibrutinib 560 mg QD



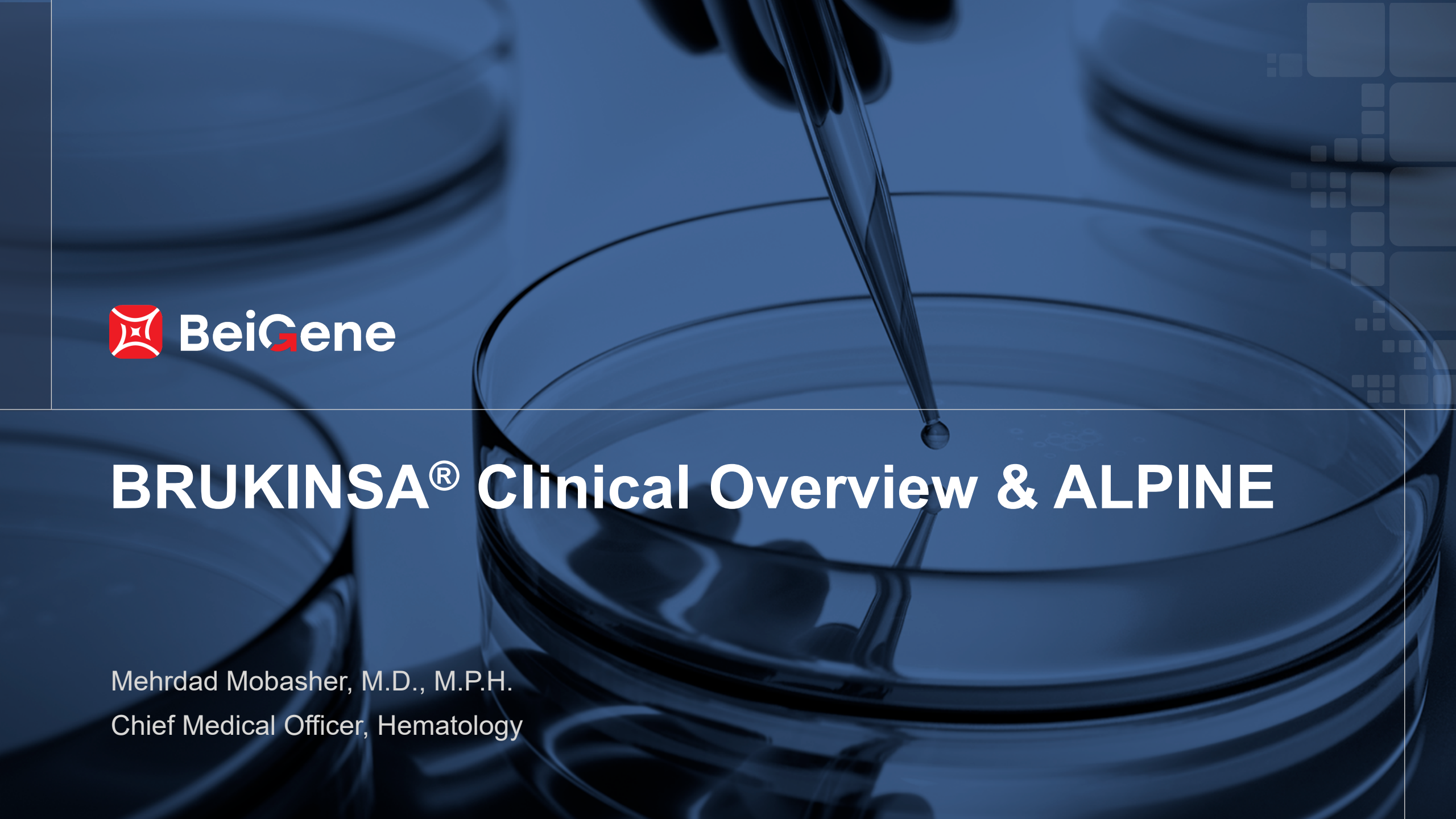
Acalabrutinib 100 mg BID



These data are from separate analyses. Limitations of cross-trial comparisons apply.

Source: 1. Kaptein, et al. *Blood.* 2018;132:1871. 2. Ou, et al. *Leuk Lymphoma.* In press. 3. Marostica, et al. *Cancer Chemother Pharmacol.* 2015;75:111-121.0

QD, Quaque Die; BID, Bis in die



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BRUKINSA® Clinical Overview & ALPINE

Mehrdad Mobasher, M.D., M.P.H.
Chief Medical Officer, Hematology

BRUKINSA® (Zanubrutinib)

Zanubrutinib

Hypothesis: Sustainable Inhibition

Engineered to exhibit **high potency, bioavailability,** and **kinase selectivity** with the aim of **reducing off-target toxicities** while maintaining **high BTK inhibition**

4,700+ patients enrolled globally

Safety and efficacy of **zanubrutinib** assessed in numerous indications **across the globe, in 30+ trials**

Two major phase 3 head-to-head trials against ibrutinib

ORR and **PFS** in **R/R CLL/SLL** patients receiving **zanubrutinib** shown to be superior to **ibrutinib** in **ALPINE**

WM patients receiving zanubrutinib showed a consistent trend of **deeper** and **more durable** responses than ibrutinib-treated patients in **ASPEN** though not significant at primary analysis

Approvals in 60+ markets across 4 indications

4 lead indications: **CLL/SLL, WM, MCL, MZL**

60+ approvals including US, EU, UK, China, Australia, Canada, South Korea and others

Expanding clinical development program

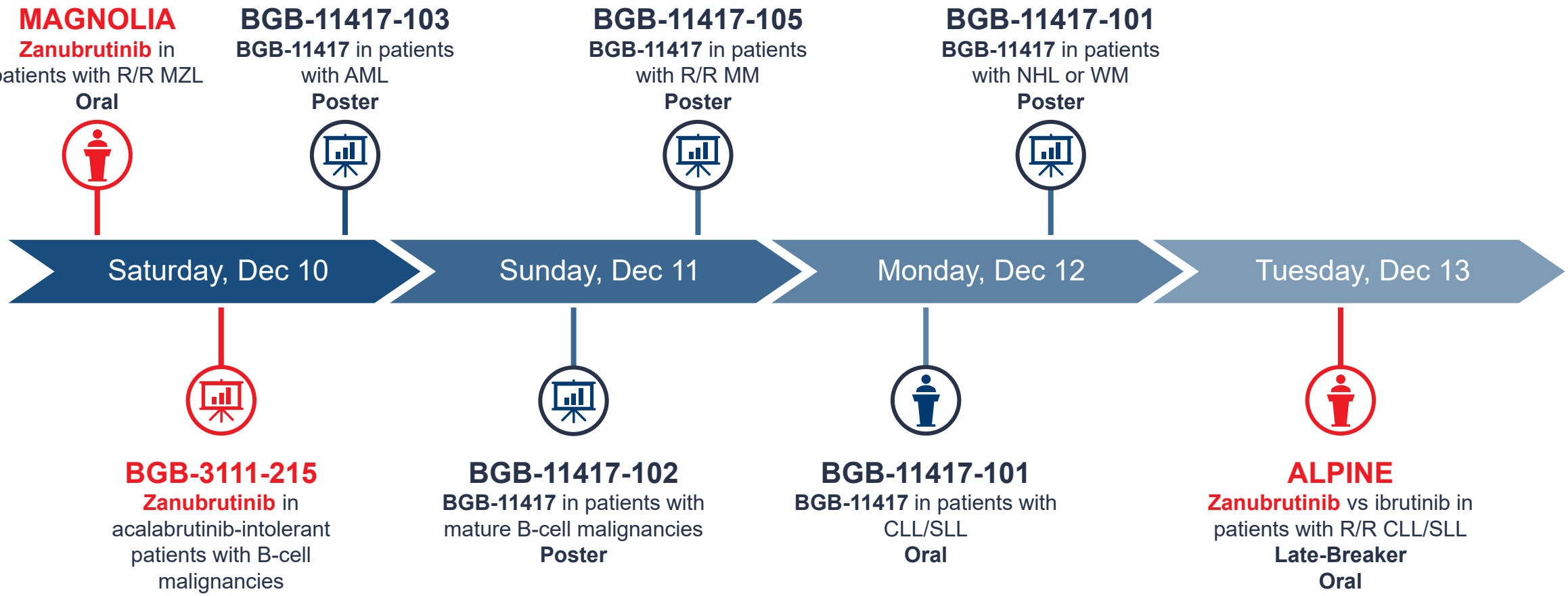
Investigation in **novel combinations** with both external collaborator compounds and **BeiGene-developed compounds** across a broad swathe of hematologic malignancies including FL

Zanubrutinib Development Overview

CLL/SLL	Phase 3	**Approved** for use in R/R CLL/SLL in China, and in 1L and R/R in the EU FDA filing for 1L and R/R CLL/SLL submitted (January 2023 PDUFA) Phase 3 **ALPINE** (R/R CLL/SLL) and **SEQUOIA** (1L CLL/SLL)
MZL	Phase 3	**Approved** for use in R/R MZL in US, Canada, and the EU Phase 3 **MAHOGANY** investigating zanubrutinib + rituximab in 1L MZL
MCL	Phase 3	**Approved** for use in R/R MCL across many regions Phase 3 **MANGROVE** investigating zanubrutinib + rituximab in 1L MCL
WM	Phase 3	**Approved** for use across many regions Exploratory long-term follow-up from the Phase 3 **ASPEN** trial demonstrated clinically meaningful efficacy and safety advantages of zanubrutinib in patients with WM
FL	Phase 2	Under investigation in combination with obinutuzumab (**ROSEWOOD** trial) and with rituximab (BGB-3111-213) in R/R FL
DLBCL	Phase 2	Under investigation as monotherapy (BGB-3111-207) or combination with rituximab (BGB-3111-213) or rituximab + lenalidomide (BGB-3111-110) in R/R DLBCL

ASH Highlights

Late Breaker, 3 Orals and 10 Posters



ABSTRACT INFORMATION

Jennifer R. Brown, MD, PhD[1], Barbara Eichhorst, MD[2], Peter Hillmen, MD PhD[3], Nicole Lamanna, MD[4], Susan M. O'Brien, MD[5], Constantine S. Tam, MBBS, MD[6,7], Lugui Qiu, MD[8], Maciej Kaźmierczak, MD, PhD[9], Wojciech Jurczak, MD, PhD[10], Keshu Zhou, MD, PhD[11], Martin Simkovic MD, PhD[12,13], Jiri Mayer, MD[14], Amanda Gillespie-Twardy, MD[15], Alessandra Ferrajoli, MD[16], Peter S. Ganly, BMBCh, PhD[17], Robert Weinkove, MBBS, PhD[18,19], Sebastian Grosicki, MD, PhD[20], Andrzej Mital, MD, PhD[21], Tadeusz Robak, MD, PhD[22], Anders Osterborg, MD, PhD[23,24], Habte A. Yimer, MD[25], Tommi Salmi, MD[26], Megan (Der Yu) Wang, PharmD[26], Lina Fu, MS[26], Jessica Li, MS[26], Kenneth Wu, PhD[26], Aileen Cohen, MD, PhD[26], Mazyar Shadman, MD, MPH[27,28]

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Tuesday, December 13, 2022: 9:00-10:30 AM
Late-Breaking Abstracts Session

Zanubrutinib Demonstrates Superior Progression Free Survival Compared with Ibrutinib for Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Results from Final Analysis of ALPINE Randomized Phase 3 Study

64th ASH Annual Meeting and Exposition,
December 10-13, 2022 **LBA #6**

Patient Demographics and Baseline Disease Characteristics

ALPINE PFS Final Analysis – R/R CLL/SLL

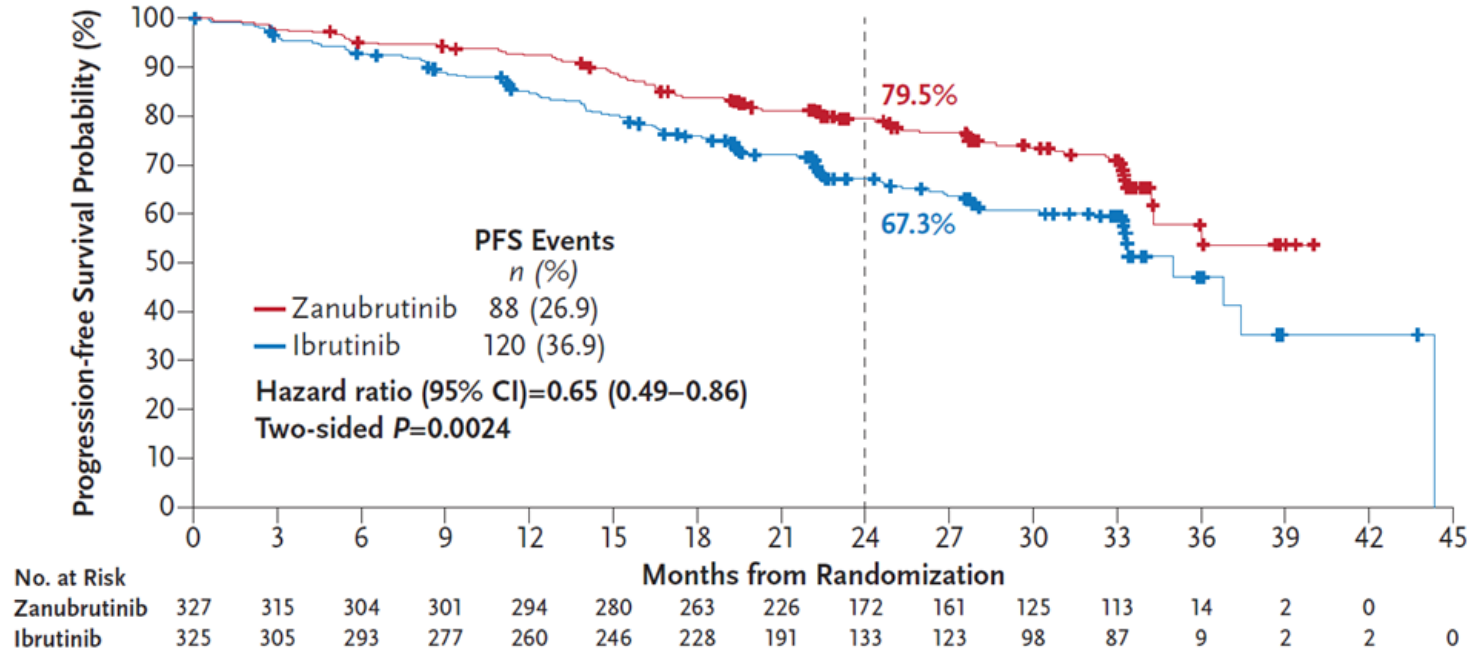
	Zanubrutinib (N=327)	Ibrutinib (N=325)
Median age	67 years	68 years
Age ≥65 years	61.5%	61.5%
Male	65.1%	71.4%
Median prior lines of therapy	1	1
Unmutated IGHV	73.1%	73.5%
Del(17p)	13.8%	15.4%
***TP53* mutation without del(17p)**	9.2%	7.7%

- Patients (N=652) from 15 countries were randomized to receive zanubrutinib (n=327) or ibrutinib (n=325)
- Demographic and disease characteristics were balanced between zanubrutinib and ibrutinib

Data cut-off: 8 Aug 2022
Brown J et al. Oral presentation presented at ASH 2022

IRC-Assessed PFS (ITT Population)

ALPINE PFS Final Analysis – R/R CLL/SLL

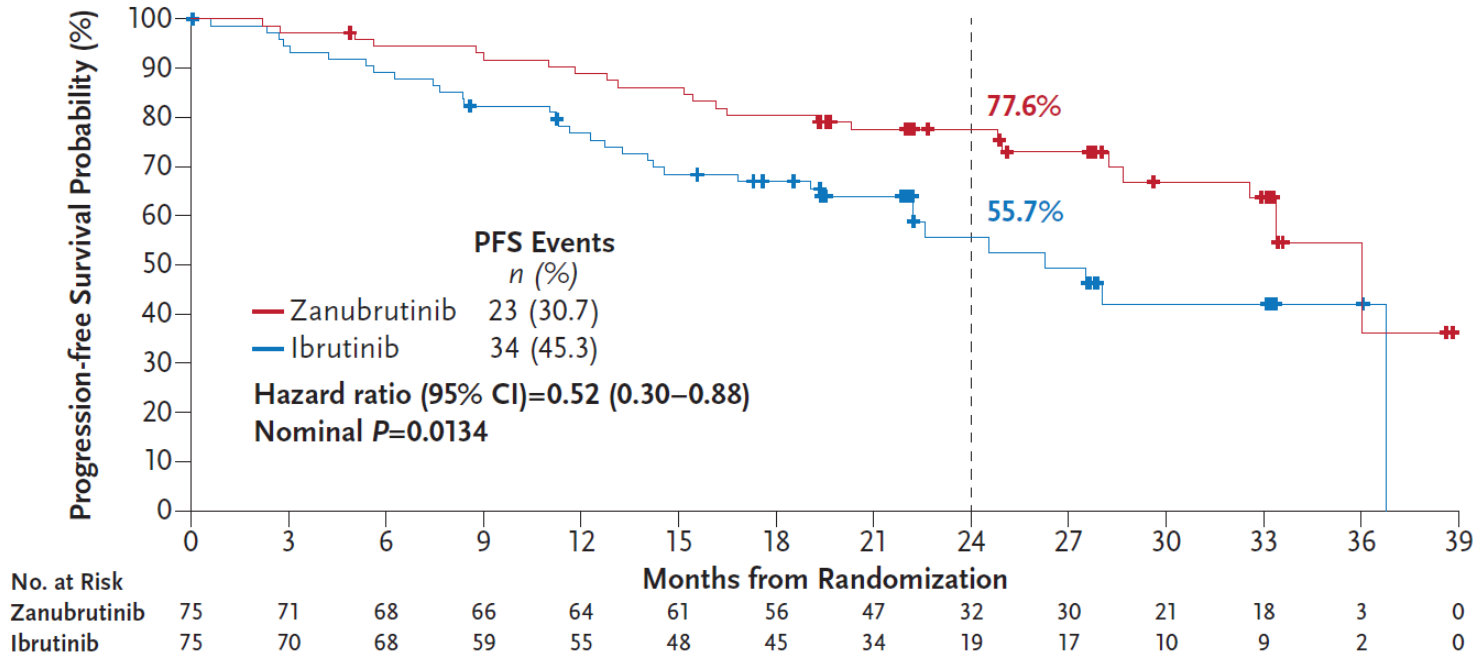


- With a median follow-up of 29.6 months, zanubrutinib PFS_{IRC}, was superior to ibrutinib in the ITT population (HR: 0.65 [95% CI, 0.49-0.86]; 2-sided *P*=.0024)
  - Identical statistical values were reported when assessed by investigator

Data cut-off: 8 Aug 2022
CI=confidence interval, HR=hazard ratio, IRC=independent review committee, ITT=intention-to-treat, PFS=progression-free survival, PFS_{IRC}=progression-free survival as assessed by IRC,
Brown J et al. Oral presentation presented at ASH 2022

IRC-Assessed PFS in Patients With del(17p)/*TP53* Mutation

ALPINE PFS Final Analysis – R/R CLL/SLL



- In a predefined subgroup of patients with del(17p)/*TP53* mutation, longer PFS_{IRC} was demonstrated with zanubrutinib than ibrutinib

Data cut-off: 8 Aug 2022
CI=confidence interval, HR=hazard ratio, IRC=independent review committee, ITT=intention-to-treat, PFS=progression-free survival, PFS_{IRC}=progression-free survival as assessed by IRC,
Brown J et al. Oral presentation presented at ASH 2022

Safety and Tolerability

ALPINE PFS Final Analysis – R/R CLL/SLL

	Zanubrutinib (N=327)	Ibrutinib (N=325)
Grade ≥3 AEs	67.3%	70.4%
Serious AEs	42.0%	50.0%
Treatment discontinuation rate	26.3%	41.2%
Discontinuation due to AEs	16.2%	22.8%
Discontinuation due to PD	7.3%	12.9%
Dose interruption	50.0%	56.8%
Dose reduction	12.3%	17.0%

- **Rate of atrial fibrillation/flutter** was lower with zanubrutinib compared with ibrutinib (5.2% vs 13.3%)
- There were no **grade 5 AEs due to cardiac disorders** with zanubrutinib vs 6 (1.9%) with ibrutinib
- **Discontinuation** rates due to cardiac disorders were 0.3% vs 4.3%

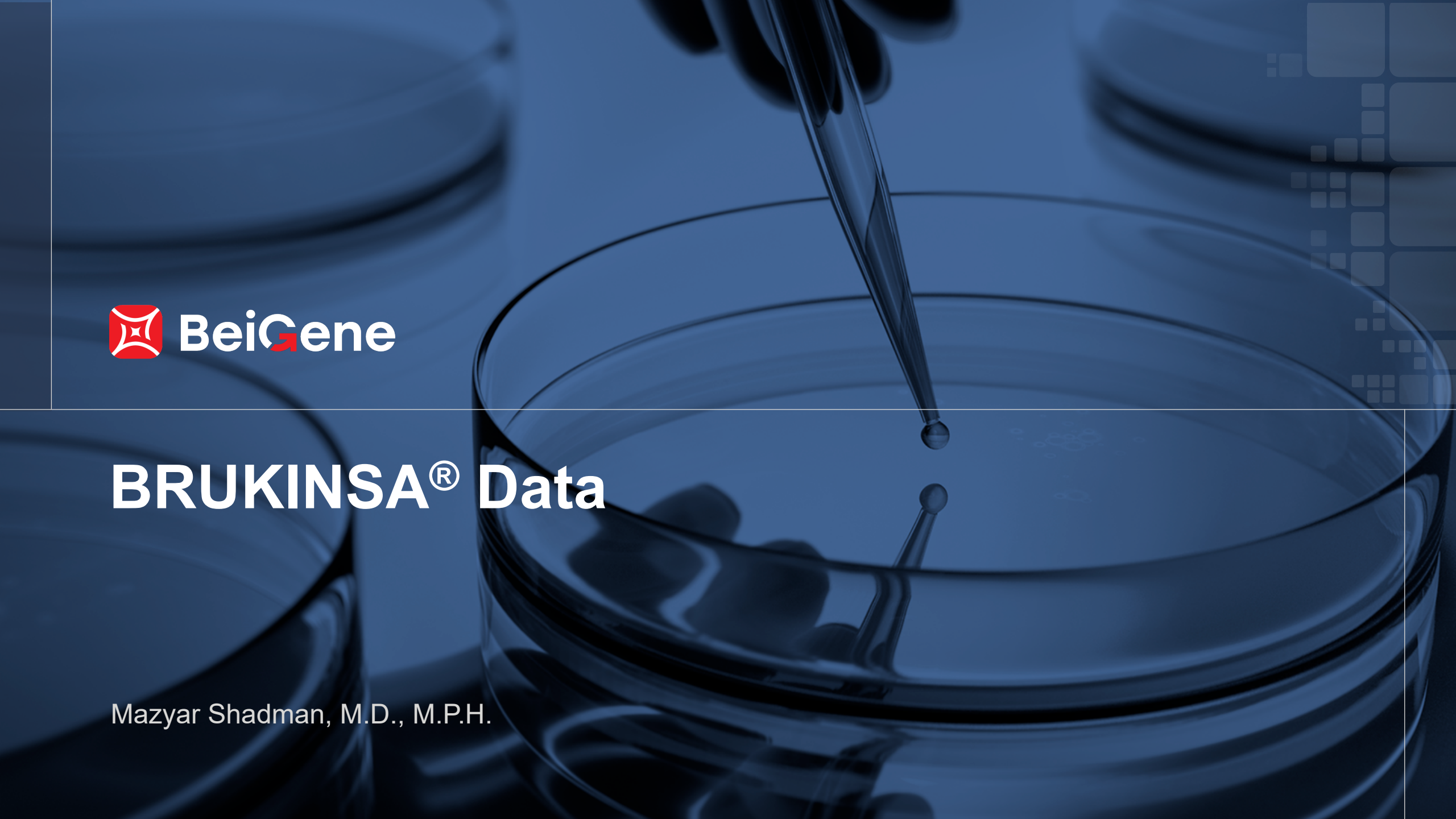
Data cut-off: 8 Aug 2022
AE=adverse event, PD=progressive disease, PFS=progression-free survival,
Brown J et al. Oral presentation presented at ASH 2022

Author Conclusions

ALPINE PFS Final Analysis – R/R CLL/SLL

- As ALPINE is the first study to demonstrate PFS superiority in a head-to-head comparison of BTK inhibitors, zanubrutinib has now proven superiority to ibrutinib in both ORR and PFS in patients with R/R CLL/SLL
- Efficacy benefits with zanubrutinib were observed across all major subgroups, including high-risk patients
- Zanubrutinib had a favorable safety profile compared with ibrutinib, with a lower rate of treatment discontinuation and fewer cardiac disorder events including fewer cardiac events leading to death
- These data suggest zanubrutinib is more efficacious and better tolerated than ibrutinib as treatment for R/R CLL/SLL

Data cut-off: 8 Aug 2022
BTK=Bruton's tyrosine kinase, CLL=chronic lymphocytic leukemia, ORR=overall response rate, PFS=progression-free survival, R/R=relapsed/refractory, SLL=small lymphocytic lymphoma,
Brown J et al. Oral presentation presented at ASH 2022



BeiGene

BRUKINSA® Data

Mazyar Shadman, M.D., M.P.H.

Mazyar Shadman, M.D., M.P.H

Associate Professor, Fred Hutch Cancer Center and University of Washington

- Dr. Shadman focuses on lymphoid malignancies with a clinical research goal to identify the best treatment sequence or combination for patients with high-risk lymphoma and CLL.
- Attending Physician, Hematologic Malignancies
  Fred Hutchinson Cancer Center
- Associate Professor, Medical Oncology Division
  University of Washington School of Medicine

Education

- Hematology and Medical Oncology fellowship, University of Washington/Fred Hutchinson Cancer Research Center,
  2011-2014
- Internal Medicine Residency, Cleveland Clinic, 2008-2011
- M.P.H., Cancer Epidemiology, University of Washington, 2008
- M.D., Tehran University of Medical Sciences, 2004

Long-Term Efficacy and Safety of Zanubrutinib in Patients With Relapsed/Refractory Marginal Zone Lymphoma (MZL): Final Analysis of the MAGNOLIA (BGB-3111-214) Trial

Stephen Opat,[1] Alessandra Tedeschi,[2] Bei Hu,[3] Kim M. Linton,[4] Pamela McKay,[5] Sophie Leitch,[6] Jie Jin,[7] Mingyuan Sun,[8] Magdalena Sobieraj-Teague,[9] Pier Luigi Zinzani,[10] Peter Browett,[11] Xiaoyan Ke,[12] Craig A. Portell,[13] Catherine Thieblemont,[14] Kirit Ardeshna,[15] Fontanet Bijou,[16] Patricia Walker,[17] Eliza A. Hawkes,[18] Shir-Jing Ho,[19] Keshu Zhou,[20] Zhiyu Liang,[21] Jianfeng Xu,[21] Chris Tankersley,[21] Richard Delarue,[21] Melannie Co,[21] and Judith Trotman[22]

[1]Monash Health and Monash University, Clayton, Victoria, Australia; [2]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy; [3]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [4]Manchester Cancer Research Centre, Division of Cancer Sciences, Manchester, UK; [5]Beatson West of Scotland Cancer Centre, Glasgow, UK; [6]North Shore Hospital, Auckland, New Zealand; [7]The First Affiliated Hospital, Zhejiang University, Hangzhou, Zhejiang, China; [8]Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China; [9]Flinders Medical Centre, Bedford Park, South Australia, Australia; [10]Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy; [11]Auckland City Hospital, Grafton, New Zealand; [12]Peking University Third Hospital, Beijing, China; [13]University of Virginia, Comprehensive Cancer Center, Charlottesville, VA, USA; [14]APHP, Hôpital Saint-Louis, Hemato-oncology, Paris University Diderot, Paris, France; [15]University College London Hospitals, London, UK; [16]Institut Bergonié, Bordeaux, France; [17]Peninsula Private Hospital, Frankston, Victoria, Australia; [18]Box Hill Hospital, Box Hill, Victoria, Australia; [19]St. George Hospital, Kogarah, New South Wales, Australia; [20]Henan Cancer Hospital, Zhengzhou, Henan, China; [21]BeiGene (Beijing) Co., Ltd., Beijing, China, BeiGene Switzerland GmbH and BeiGene USA, Inc., San Mateo, CA, USA; and [22]Concord Repatriation General Hospital, University of Sydney, Concord, New South Wales, Australia

Saturday, December 10, 2022 (2:00 PM - 3:30 PM)
623. Mantle Cell, Follicular, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological

64th ASH Annual Meeting and Exposition,
December 10-13, 2022 **Abstract 234**

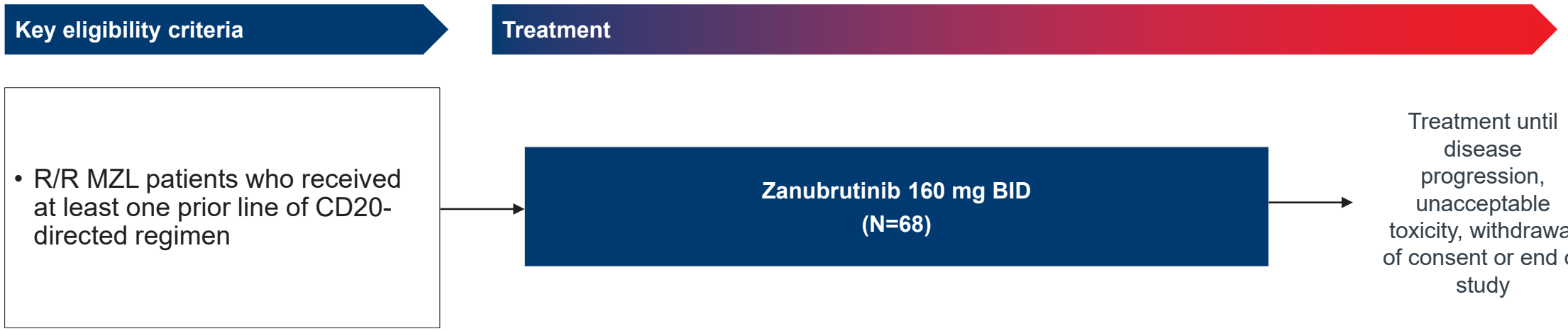
Study Design

MAGNOLIA Final Analysis – R/R MZL

Phase 2

Study identifier: BGB-3111-214, NCT03846427

Primary endpoint: ORR assessed by IRC according to Lugano classification 2014[3]
Key secondary endpoints: ORR by PI, PFS, OS, DOR, safety



- Response based on the Lugano classification for NHL[3]
  - PET-based criteria for patients with IRC-confirmed FDG-avid disease
  - CT-based criteria for non-FDG-avid patients
  - Additional sensitivity analysis for all evaluable patients using CT-based criteria
- Biomarker correlative sub-study by the Australasian Leukaemia and Lymphoma Group

BID=twice a day, CD=cluster of differentiation, CT=computed tomography, DOR=duration of response, FDG=fluorodeoxyglucose, IRC=independent review committee, MZL=marginal zone lymphoma, ORR=overall response rate, OS=overall survival, PFS=progression-free survival, PI=principal investigator, R/R=relapsed/refractory.

1. Opat S et al. Oral presentation presented at ASH 2022. Abstract 234 2. Opat S et al. ASH 2020. Abstract 339. 3. Cheson BD et al. J Clin Oncol. 2014;32:3059–3067. This study is registered at ClinicalTrials.gov (NCT03846427).

Baseline Demographics and Disease History

MAGNOLIA Final Analysis – R/R MZL

Characteristics, n (%)	Total (N=68)
Median age (range), years	70 (37-95)
≥65	41 (60)
≥75	19 (28)
Male	36 (53)
ECOG PS 0/1[a]	63 (93)
MZL subtypes	
Extranodal	26 (38)
Nodal	26 (38)
Splenic	12 (18)
Unknown	4 (6)

Characteristics, n (%)	Total (N=68)
Disease status	
Relapsed	44 (65)
Refractory	22 (32)
Stage III/IV	59 (87)
FDG-avid (by IRC)	61 (90)
Extranodal site involvement	53 (78)
Bone marrow infiltration	29 (43)
Median prior lines of systemic therapy (range)	2 (1-6)
Immunochemotherapy	61 (90)[b]
Rituximab monotherapy	7 (10)

Data cutoff date: 04 May 2022.
aOverall, 43% of patients had ECOG 1/2. bRituximab-based chemotherapy in most patients (n=60; 88%).
ECOG=Eastern Cooperative Oncology Group, FDG=fluorodeoxyglucose, IRC=independent review committee, MZL=marginal zone lymphoma, PS=performance status,
Opat S et al. Oral presentation presented at ASH 2022. Abstract 234

Best Overall Response by IRC and Investigator Assessment

MAGNOLIA Final Analysis – R/R MZL

Efficacy	(N=66)[a]		
	IRC		INV
	PET and/or CT (primary endpoint)[b]	CT only (sensitivity analysis)[f]	PET and/or CT
ORR, n (%) [95% CI] P-value	45 (68) [55.6, 79.1] <0.0001[c]	44 (67) [54.0, 77.8]	50 (76) [63.6 85.5]
Best response, n (%)			
CR	17 (26)	16 (24)	19 (29)
PR	28 (42)	28 (42)	31 (47)
SD	14 (21)[d,e]	16 (24)	10 (15)
PD	6 (9)	5 (8)	5 (8)
Discontinued study prior to 1st assessment, n (%)	1 (1)	1 (1)	1 (1)
Median time to response (range), months	2.8 (1.7-11.1)	3.0 (1.8-22.2)	2.8 (1.7-16.6)

Data cutoff date: 04 May 2022.
aTwo patients were excluded from the efficacy population owing to lack of central confirmation of MZL. bPatients with IRC-confirmed FDG-avid disease were assessed by PET-based criteria; non–FDG-avid patients were assessed by CT-based Lugano criteria. cP-value for the primary endpoint was computed with the binomial exact test against the null hypothesis of ORR = 30% with alternative of ORR > 30%. dFive (7.6%) patients with stable disease are remaining on study treatment (after 12-18 cycles). eIncludes one patient with FDG-avid disease who missed the PET scan at cycle 3 and was assessed as non-PD; CT showed stable disease at cycle 3. fAdditional sensitivity analysis using CT-based Lugano criteria for all 66-evaluable patients regardless of PET status at baseline.
CI=confidence interval, CR=complete response, CT=computed tomography, INV=investigator, IRC=independent review committee, ORR=overall response rate, PD=progressive disease, PET=positron emission tomography, PR=partial response, SD=stable disease,
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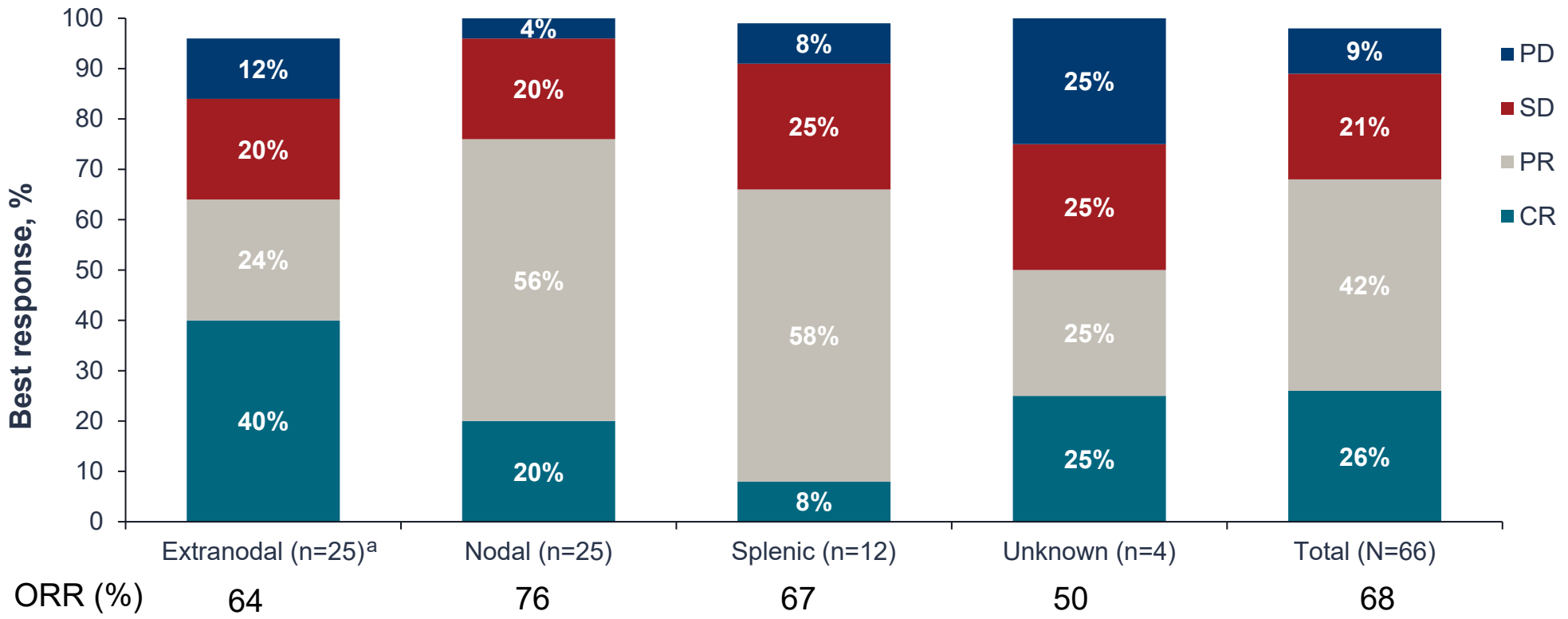
Best Overall Response by IRC and MZL Subtypes

MAGNOLIA Final Analysis – R/R MZL



Data cutoff date: 04 May 2022.
aOne patient (extranodal MZL) who withdrew consent prior to the first disease assessment was not shown in the graph.
CR=complete response, ORR=overall response rate, PD=progressive disease, PR=partial response, SD=stable disease,
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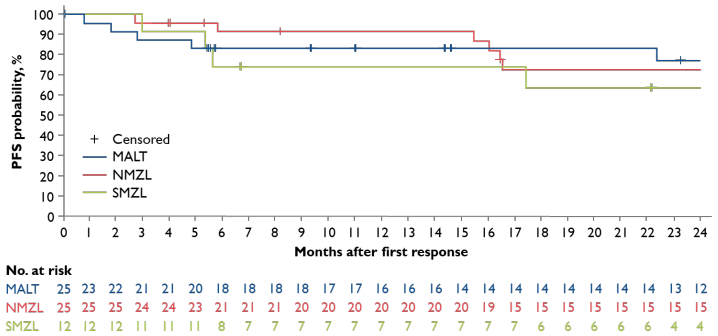
PFS, DoR, and OS by MZL Subtypes

MAGNOLIA Final Analysis – R/R MZL

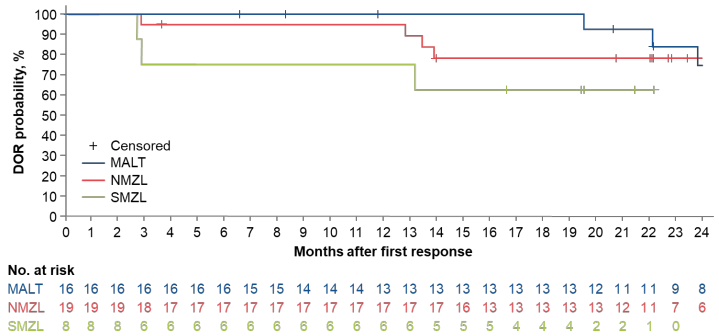
Progression-Free Survival (IRC Assessment)



PFS rate at 24 months:

Overall	**71%**
MALT	77%
NMZL	73%
SMZL	64%

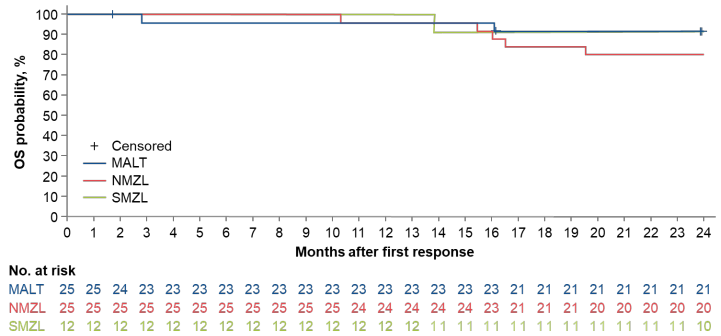
Duration of Response (IRC Assessment)



DoR rate at 24 months:

Overall	**73%**
MALT	75%
NMZL	78%
SMZL	NE

Overall Survival



OS rate at 24 months:

Overall	**86%**
MALT	92%
NMZL	80%
SMZL	92%

- PFS, DoR, and OS rates at 24 months were comparable between MZL subtypes

Data cutoff date: 04 May 2022.
DoR=duration of response, IRC=independent review committee, MALT=mucosa-associated lymphoid tissue, MZL=marginal zone lymphoma, NMZL=nodal marginal zone lymphoma, PFS=progression-free survival, SMZL=splenic marginal zone lymphoma,
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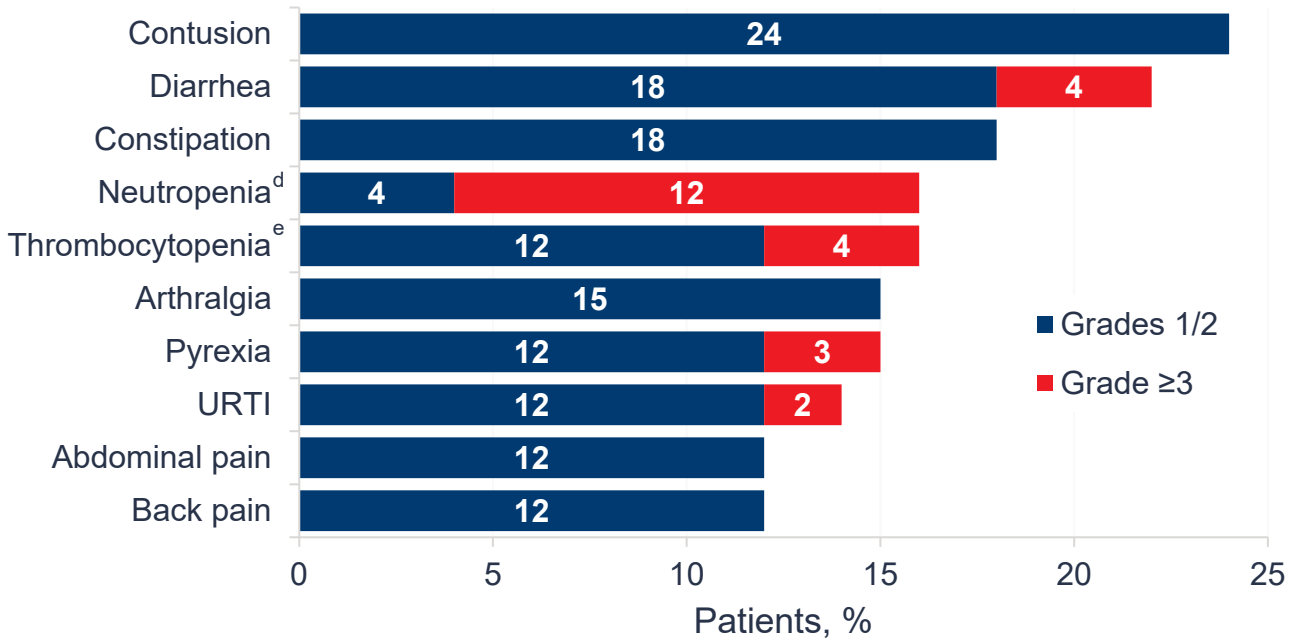
TEAEs in All Patients

MAGNOLIA Final Analysis – R/R MZL

Safety Summary

TEAEs, n (%)	N=68
Patients with ≥1 TEAE	68 (100)
Grade ≥3 TEAE	33 (48)
Serious TEAE	30 (44)
Leading to death	5 (7)[a]
Leading to dose interruption	25 (37)[b]
Leading to study drug discontinuation	5 (7)[c]
Leading to dose reduction	0

Most Common TEAEs



Data cutoff date: 04 May 2022.
aFive patients died owing to AEs: COVID-19 pneumonia (n=2); myocardial infarction in a patient with preexisting cardiovascular disease (n=1); acute myeloid leukemia in a patient with prior exposure to an alkylating agent (n=1); septic encephalopathy following radical cystectomy and ileal conduit in a patient with recurrent bladder cancer (in CR at the time of death; [n=1]). bMost common AEs leading to dose interruption: COVID-19 pneumonia (n=4), neutropenia (n=3), diarrhea (n=2), lower respiratory tract infection (n=2), pneumonia (n=2), pyrexia (n=2), syncope (n=2), and tonsillitis (n=2). cFive patients discontinued owing to AEs: COVID-19 pneumonia (n=2); pyrexia later attributed to disease progression (n=1); myocardial infarction (n=1); septic encephalopathy (n=1). dIncludes neutropenia and neutrophil count decreased. eIncludes thrombocytopenia and platelet count decreased
TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.
TEAE=treatment emergent adverse event, URTI=upper respiratory tract infection,
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TEAEs of Clinical Interest

MAGNOLIA Final Analysis – R/R MZL

TEAEs of interest, n (%)	N=68	
	All grade	Grade ≥3
Infections	38 (56)	15 (22)[a]
Hemorrhage	28 (41)	1 (1.5)[b]
Cardiac		
Hypertension	3 (4)[c]	2 (3)
Atrial fibrillation/flutter	2 (3)[d]	1 (1.5)
Ventricular extrasystole	1 (1.5)[e]	0
Second primary malignancy	5 (7)[f]	3 (4)

Data cutoff date: 04 May 2022.
aFatal infection: COVID-19 pneumonia (n=2). bGastrointestinal hemorrhage (day 862) in a patient who also received anticoagulant for pulmonary embolism; patient continued zanubrutinib with no recurrent bleeding episode. cTwo 2 patients had new-onset hypertension; none led to treatment reduction or discontinuation. dAtrial fibrillation in a patient with preexisting atrial fibrillation (21 days after end of treatment owing to disease progression). Patient with atrial flutter recovered spontaneously and continued zanubrutinib. eVentricular extrasystole in an 83-year-old patient with no known cardiac history, was non-serious, transient, resolved on the same day, and did not lead to treatment modification or discontinuation. fIncludes basal cell and squamous cell carcinoma and basal cell carcinoma (with history of skin cancer); papillary thyroid carcinoma; (with preexisting thyroid nodule); recurrent bladder cancer and prostate cancer (with history of bladder cancer); and acute myeloid leukemia (with prior chemotherapy with alkylating agent).
COVID=coronavirus disease, TEAE=treatment emergent adverse event,
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Cardiac TEAEs of Clinical Interest

MAGNOLIA Final Analysis – R/R MZL

Cardiovascular disorders, n (%)	MAGNOLIA Zanubrutinib (n=68)
Median treatment duration, months	24
Any cardiovascular medical history	
Atrial fibrillation/flutter	8 (11.7)
Ventricular arrhythmia[a]	0
Hypertension[b]	21 (30.9)
Any cardiovascular AE	
Atrial fibrillation/flutter	2 (3)
Ventricular arrhythmia (grade ≥2)[a]	1 (1.5)
Hypertension[b]	3 (4)

Data cutoff date: 04 May 2022.
aIncluding ventricular tachyarrhythmia (SMQ narrow), ventricular arrhythmias and cardiac arrest (High Level Term MeDRA v24.0). bIncluding hypertension (SMQ narrow). cPooled analyses of 10 clinical studies of zanubrutinib.[1]
AE=adverse event, CTCAE=Common Terminology Criteria for Adverse Events, EAIR=exposure-adjusted incidence rate, MeDRA=Medical Dictionary for Regulatory Activities, SMQ=standardized MedDRA query,
1. Tam et al. LL&M 2022. Abstract 1324736.
Opat S et al. Oral presentation presented at ASH 2022. Abstract 234

Cardiac TEAEs of Clinical Interest

MAGNOLIA Final Analysis – R/R MZL

Cardiovascular disorders, n (%)	MAGNOLIA	Pooled analysis B-cell malignancies[c]	
	Zanubrutinib (n=68)	Zanubrutinib (N=1550)	Ibrutinib (N=422)
Median treatment duration, months	24	26.64	19.96
Any cardiovascular medical history			
Atrial fibrillation/flutter	8 (11.7)	101 (6.5)	26 (6.2)
Ventricular arrhythmia[a]	0	14 (0.9)	1 (0.2)
Hypertension[b]	21 (30.9)	669 (43.2)	206 (48.8)
Any cardiovascular AE			
Atrial fibrillation/flutter	2 (3)	60 (3.9)	60 (14.2)
		EAIR: 0.13 vs 0.82 person-month ($p < 0.0001$)	
Ventricular arrhythmia (grade ≥2)[a]	1 (1.5)	11 (0.7)	6 (1.4)
Hypertension[b]	3 (4)	225 (14.5)	85 (20.1)

Data cutoff date: 04 May 2022.
aIncluding ventricular tachyarrhythmia (SMQ narrow), ventricular arrhythmias and cardiac arrest (High Level Term MeDRA v24.0). bIncluding hypertension (SMQ narrow). cPooled analyses of 10 clinical studies of zanubrutinib.[1]
AE=adverse event, CTCAE=Common Terminology Criteria for Adverse Events, EAIR=exposure-adjusted incidence rate, MeDRA=Medical Dictionary for Regulatory Activities, SMQ=standardized MedDRA query,
1. Tam et al. LL&M 2022. Abstract 1324736.
Opat S et al. Oral presentation presented at ASH 2022. Abstract 234

Author Conclusions

MAGNOLIA Final Analysis – R/R MZL

- At a median study follow-up of 28 months:
  - Zanubrutinib showed high response rates and durable disease control in R/R MZL
    - ORR of 68% (by PET and/or CT) and 67% (by CT only) with a CR of ~25% by IRC
    - Responses in all MZL subtypes and in difficult-to-treat subgroups
    - At 24 months: PFS rate, 71%; DOR rate, 73%; OS rate, 86%

- Zanubrutinib was generally well tolerated
  - Hypertension and atrial fibrillation/flutter were uncommon; comparable rate to zanubrutinib pooled safety analyses and lower than reported for ibrutinib
  - One (1.5%) patient had major gastrointestinal hemorrhage while receiving concomitant anticoagulant
  - No new safety signals observed

Data cutoff date: 04 May 2022.
CT=computed tomography, DoR=duration of response, CR=complete response, IRC=independent review committee, MZL=marginal zone lymphoma, OS=overall survival, PET=positron emission tomography, PFS=progression-free survival, R/R=relapsed/refractory,
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Zanubrutinib in Acalabrutinib-Intolerant Patients With B-Cell Malignancies

Mazyar Shadman,[1] Ian W. Flinn,[2] Edwin C. Kingsley,[3] Benjamin Freeman,[4] Moshe Y. Levy,[5] Houston Holmes,[5] Charles M. Farber,[6] Arvind Chaudhry,[7] Rocco Crescenzo,[8] Adam Idoine,[8] Xiaoping Zhang,8 Aileen Cohen,8 Kunthel By,[8] Jane Huang,[8] and Jeff P. Sharman[9]

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Saturday, December 10, 2022
623: Mantle Cell, Follicular, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological: Poster I

64th ASH Annual Meeting and Exposition,
December 10-13, 2022 **Abstract 1587**

Study Design

BGB-3111-215 – Acalabrutinib-Intolerant Patient Cohort

PHASE 2

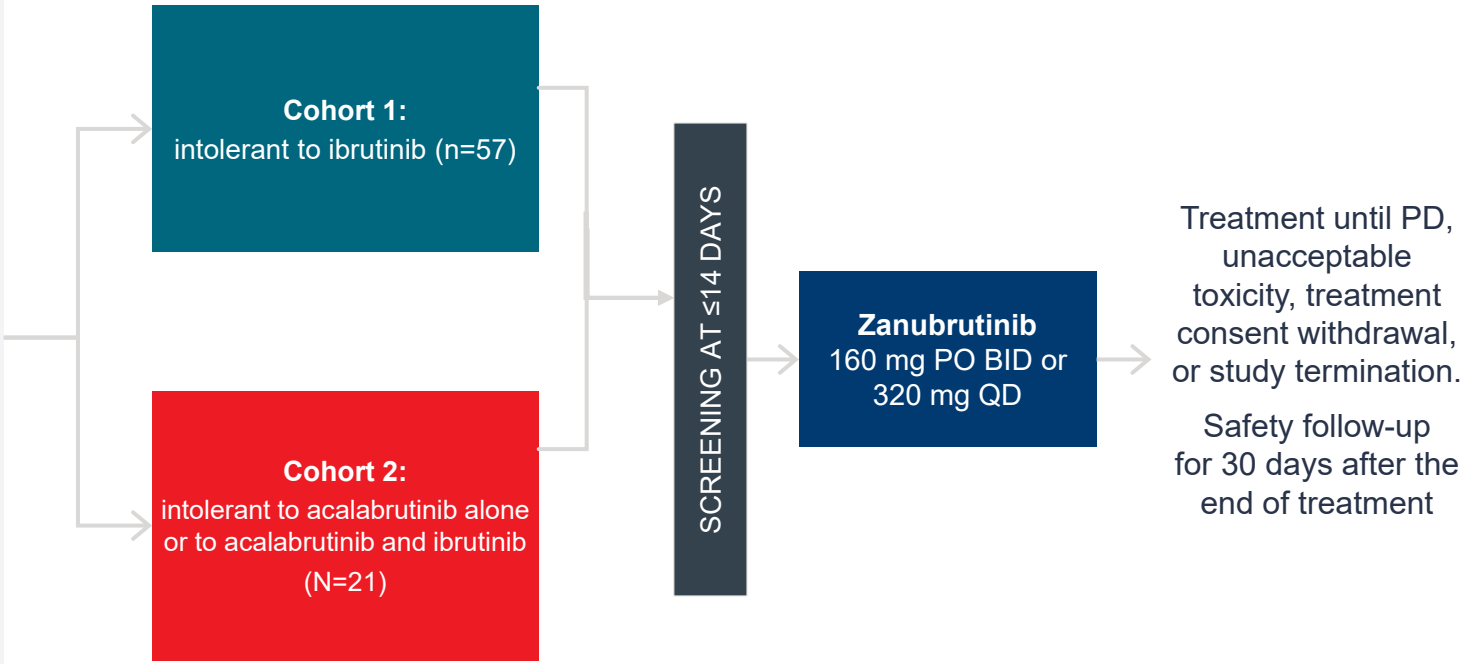
Study Identifier: BGB-3111-215, NCT04116437

Primary Endpoint: Investigator-assessed recurrence and change in severity of ibrutinib or acalabrutinib intolerance events
Key Secondary Endpoints: ORR, DCR, PFS and HRQoL

KEY ELIGIBILITY CRITERIA

- Previously treated CLL/SLL, WM, MCL or MZL patient intolerant of ibrutinib and/or acalabrutinib
- ≥18 years old
- Indication for treatment per iwCLL prior to ibrutinib
- Ibrutinib- and/or acalabrutinib intolerant in opinion of investigator

TREATMENT



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- Ibrutinib- and/or acalabrutinib intolerant in opinion of investigator

Key Inclusion Criteria for Acalabrutinib Intolerance Leading to Discontinuation

- Grade ≥1 nonhematologic toxicity for >7 days
- Grade ≥1 nonhematologic toxicity of any duration with >3 recurrent episodes
- Grade ≥3 nonhematologic toxicity for any duration
- Grade 3 neutropenia with infection or fever
- Grade 4 hematologic toxicity that persists until BTKi therapy is discontinued due to toxicity
- Inability to use acid-reducing agents or anticoagulants due to current BTKi use
- Resolution of grade ≥2 BTKi toxicities to grade ≤1 or baseline and resolution of grade 1 BTKi toxicities to grade 0 or baseline before initiating zanubrutinib treatment

TREATMENT

Cohort 1:
intolerant to ibrutinib (n=57)

Cohort 2:
intolerant to acalabrutinib alone or to acalabrutinib and ibrutinib
(N=21)

SCREENING AT ≤14 DAYS

Zanubrutinib
160 mg PO BID or
320 mg QD

Treatment until PD, unacceptable toxicity, treatment consent withdrawal, or study termination.

Safety follow-up for 30 days after the end of treatment

Patient Demographics and Baseline Characteristics

BGB-3111-215 – Acalabrutinib-Intolerant Patient Cohort

Characteristic	Cohort 2 (N=21)
Indication, n (%)	
CLL	13 (62)
SLL	2 (10)
MCL	1 (5)
MZL	2 (10)
WM	3 (14)
Age, median (range), years	73 (51-87)
Sex, n (%)	
Male	13 (62)
Female	8 (38)
ECOG PS, n (%)	
0	13 (62)
1	6 (29)
2	2 (10)

Characteristic	Cohort 2 (N=21)
No. of prior anticancer therapy regimens, median (range)	2 (1-6)
Prior BTKi, n (%)	
Ibrutinib monotherapy	10 (48)
Ibrutinib combination therapy[a]	1 (4.8)
Acalabrutinib monotherapy	20 (95)
Acalabrutinib combination therapy[a]	1 (4.8)
Cumulative acalabrutinib exposure, median (range), months	4.6 (0.2-26.9)
On-study zanubrutinib dosing regimen, n (%)	
160 mg BID	14 (67)
320 mg QD	7 (33)

Data cutoff: 1 September 2022.
aCombination therapy is defined as a regimen of 2 or more drugs that contains ibrutinib or acalabrutinib.
BID=twice daily, BTKi=Bruton's tyrosine kinase inhibitor, CLL=chronic lymphocytic leukemia, ECOG=Eastern Cooperative Oncology Group, MCL=mantle cell lymphoma, MZL=marginal zone lymphoma, PS=performance status, QD=once daily, SLL=small lymphocytic lymphoma, WM=Waldenström's macroglobulinemia,
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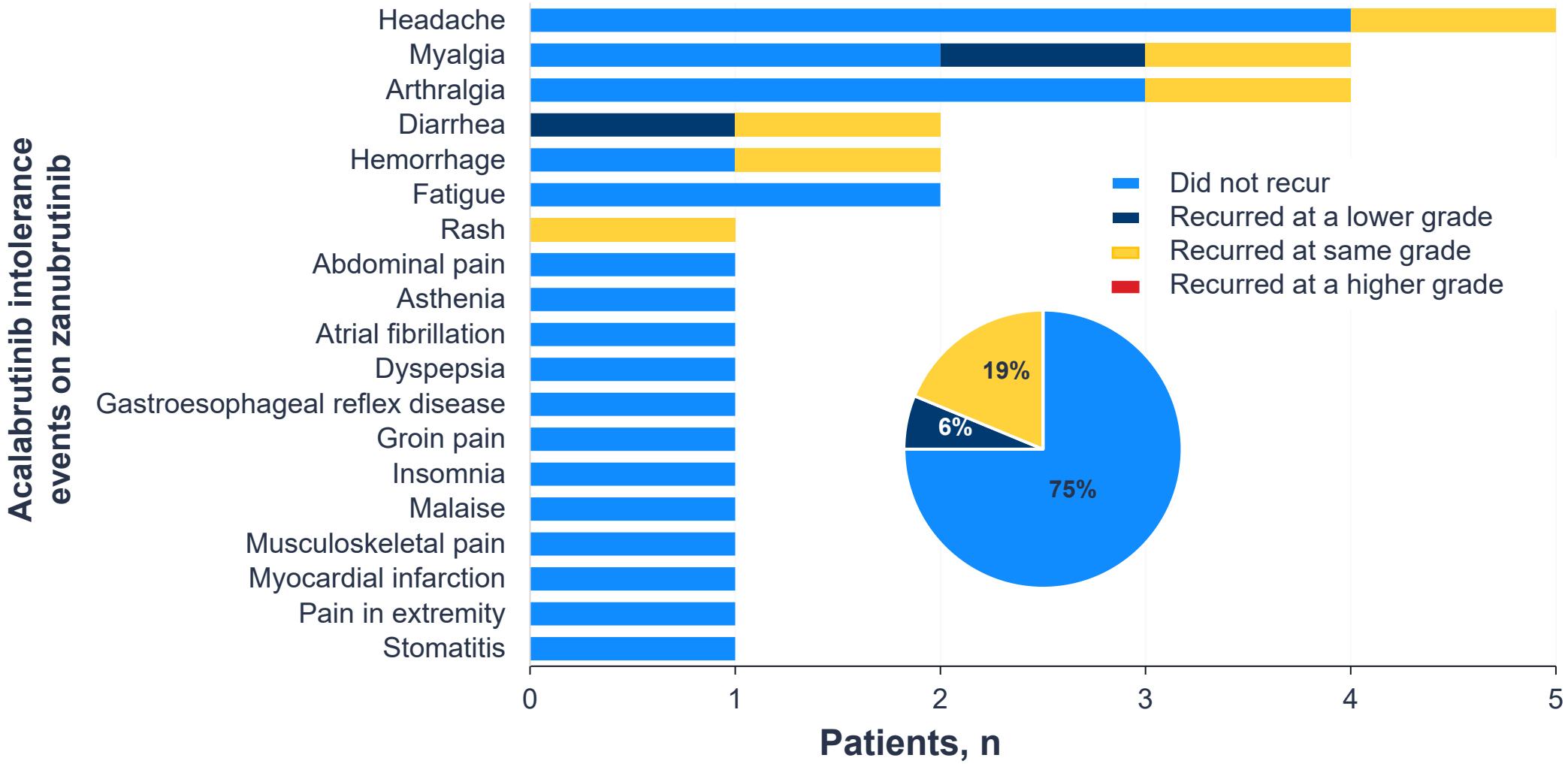
Recurrence of Acalabrutinib Intolerance Events on Zanubrutinib

BGB-3111-215 – Acalabrutinib-Intolerant Patient Cohort



Data cutoff: 1 September 2022.
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Intolerance Events

BGB-3111-215 – Acalabrutinib-Intolerant Patient Cohort

- 32 acalabrutinib intolerance events
- The most common acalabrutinib intolerances were headache (n=5), arthralgia (n=4), myalgia (n=4), diarrhea (n=2), fatigue (n=2), and hemorrhage (n=2)
- Most (24 of 32 [75%]) acalabrutinib intolerance events did not recur on zanubrutinib at any grade, and no acalabrutinib intolerance events recurred at a higher severity
- Fourteen (67%) of 21 patients did not experience any recurrence of their prior acalabrutinib intolerance events
- Two (10%) of 21 patients discontinued zanubrutinib due to recurrence of their prior acalabrutinib intolerance events (myalgia and diarrhea)
- Three (14%) of 21 patients experienced the same intolerance event (pain in extremity, diarrhea and atrial fibrillation) on ibrutinib and acalabrutinib
  - Two did not have a recurrence of those on zanubrutinib
  - One had a recurrence at lower grade (diarrhea)

Data cutoff: 1 September 2022.
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Safety Overview

BGB-3111-215 – Acalabrutinib-Intolerant Patient Cohort

AEs, n (%)	Any grade (N=21)	Grade ≥3 (N=21)
Any AE[a]	20 (95)	4 (19)[b]
Fatigue	6 (29)	0
Diarrhea	5 (24)	1 (5)
Hypertension	5 (24)	1 (5)
Arthralgia	4 (19)	0
Cough	4 (19)	0
Myalgia	4 (19)	0
COVID-19	3 (14)	1 (5)
Contusion	3 (14)	0
Decreased appetite	3 (14)	0
Dyspnoea	3 (14)	0
Night sweats	3 (14)	0
Pain in extremity	3 (14)	0

AEs, n (%)	Any grade (N=21)	Grade ≥3 (N=21)
Pyrexia	3 (14)	0
Rash	3 (14)	0
Back pain	2 (10)	0
Dizziness	2 (10)	0
Peripheral edema	2 (10)	0
Oropharyngeal pain	2 (10)	0
Palpitations	2 (10)	0
Maculopapular rash	2 (10)	0
SARS-CoV-2 test positive	2 (10)	0
Urinary tract infection	2 (10)	0
Neutrophil count decreased	2 (10)	2 (10)
Febrile neutropenia	1 (5)	1 (5)
Gastroenteritis salmonella	1 (5)	1 (5)

- The most common grade ≥3 AE was neutrophil count decreased, which occurred in 2 (10%) patients
- No atrial fibrillation, anemia, or thrombocytopenia/platelet count decreased occurred in any patient

Data cutoff: 1 September 2022.
aAny grade events occurring in ≥2 patients or grade ≥3 events occurring in ≥1 patients. bSome patients had >1 grade ≥3 event.
AE=adverse event,
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Summary of SAEs and AEs Leading to Dose Modification

BGB-3111-215 – Acalabrutinib-Intolerant Patient Cohort

AEs, n (%)	Any grade (N=21)
Serious AE	2 (10)
Leading to treatment discontinuation	2 (10)
Leading to dose interruption	11 (52)
Leading to dose reduction	3 (14)
Leading to death	0

Data cutoff: 1 September 2022.
AE=adverse event, SAE=serious adverse event,
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Best Overall Response by Investigator Assessment

BGB-3111-215 – Acalabrutinib-Intolerant Patient Cohort

- Among the 18 efficacy-evaluable patients, 17 (94%) achieved SD or better, and 11 (61%) achieved a PR or better
- Eight (67%) of 12 efficacy-evaluable patients with CLL/SLL achieved a PR or better

Response	Cohort 2 (N=18)
DCR (SD or better), n (%) (95% CI)	17 (94) (72.7, 99.9)
ORR (better than SD), n (%) (95% CI)	11 (61) (35.7, 82.7)
BOR rate, n (%)	
PR/VGPR[a]	11 (61)
SD	6 (33)
PD	1 (6)
Time to BOR, median (range), months	3 (2.7-11.1)
Time to first overall response, median (range), months	3 (2.7-11.1)

Data cutoff: 1 September 2022.
aIncludes PR or better in all patients, PR-L or better in CLL.
BOR=best overall response, CLL=chronic lymphocytic leukemia, CI=confidence interval, DCR=disease control rate, PR=partial response, SD=stable disease, SLL=small lymphocytic lymphoma, VGPR=very good partial response,
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Author Conclusions

BGB-3111-215 – Acalabrutinib-Intolerant Patient Cohort

- With a median zanubrutinib exposure of 7.6 months, longer than the reported cumulative acalabrutinib exposure before discontinuation (4.6 months), most (67%) patients did not experience any recurrence of their prior acalabrutinib intolerance events
- Zanubrutinib provided clinically meaningful benefit to 17 (94%) of 18 efficacy-evaluable patients who were previously intolerant to acalabrutinib
- These outcomes suggest that patients who are intolerant to acalabrutinib can attain clinical benefit by switching to zanubrutinib

Data cutoff: 1 September 2022.
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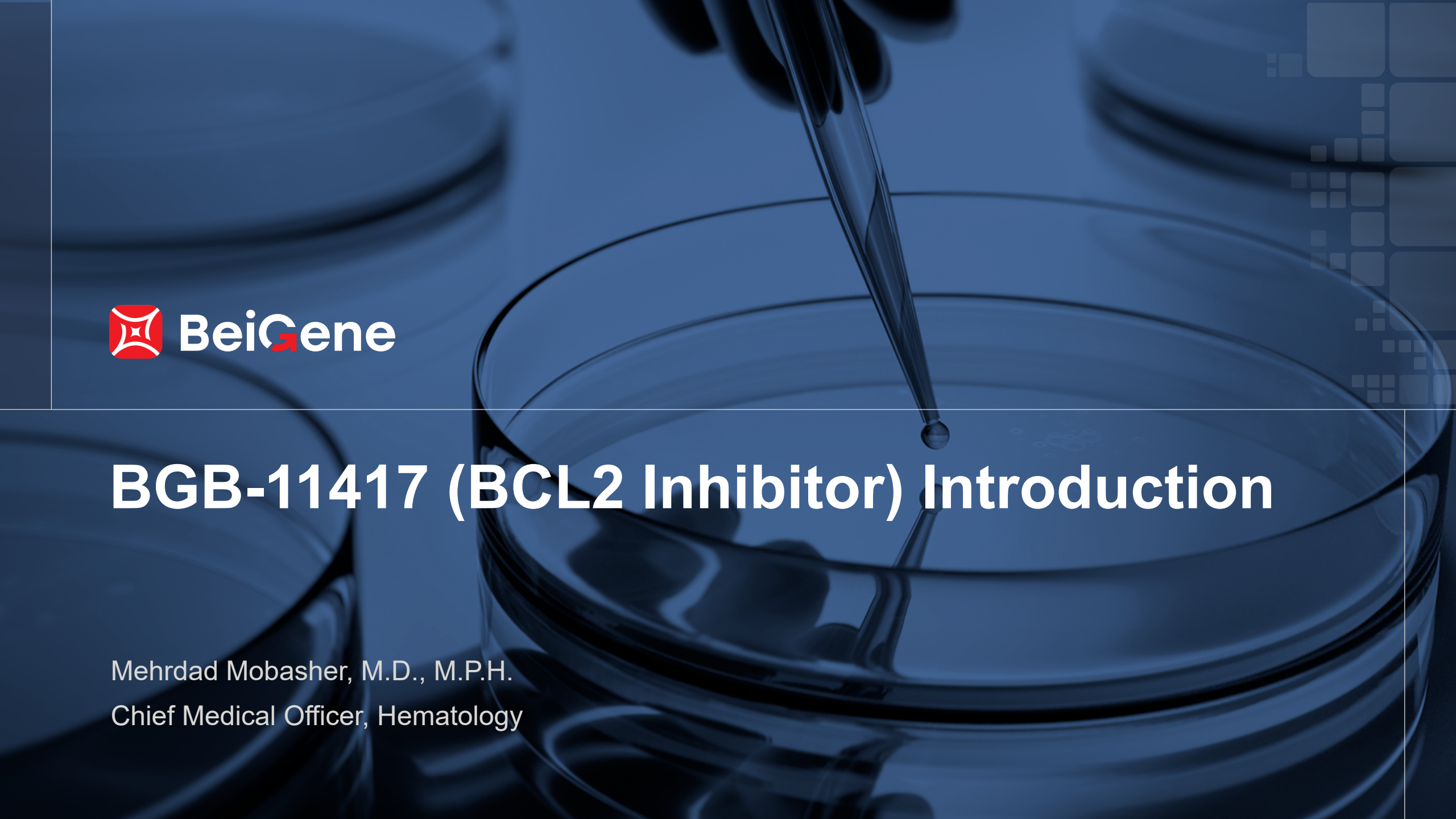


BeiGene

BGB-11417 (BCL2 Inhibitor) Introduction

Mehrdad Mobasher, M.D., M.P.H.
Chief Medical Officer, Hematology

BCL-2i Program Summary

- BGB-11417 is a BCL2 inhibitor with potential to be best in class given higher potency and increased selectivity as well as shorter half-life compared to venetoclax that can potentially lead to improved efficacy and safety.
- Broad development plan initiated in CLL, NHL (including WM, MCL, MZL), AML, MDS and MM.
- With more than 300 patients treated to date in 4 phase 1 studies, no safety concerns.
- Encouraging early efficacy in all indications eg. durable and deep responses seen in CLL at all doses tested- longer follow up is needed for higher dose. AML patients on BGB-11417 + azacitidine have high rates of blast clearance with doses as low as 40mg and responses are durable.
- Two trials with registrational intent:
  - **R/R MCL** after failure of BTKi
  - **R/R CLL** after failure of BTKi
- Broad registrational opportunities:

BGB-11417: A More Potent and Selective BCL-2 Inhibitor Compared to Venetoclax

Potentially translating to deeper target inhibition/better efficacy, less off-target effects -->better safety, and the potential for overcoming acquired resistance to venetoclax (G101V)

Highly potent

	Protein IC50 (nM)	
	BCL-2	BCL-2 G101V
BGB-11417	0.014 ± 0.0021	0.59 ± 0.08
	1:14	1:57
Venetoclax	0.20 ± 0.015	34 ± 3.8

Highly selective

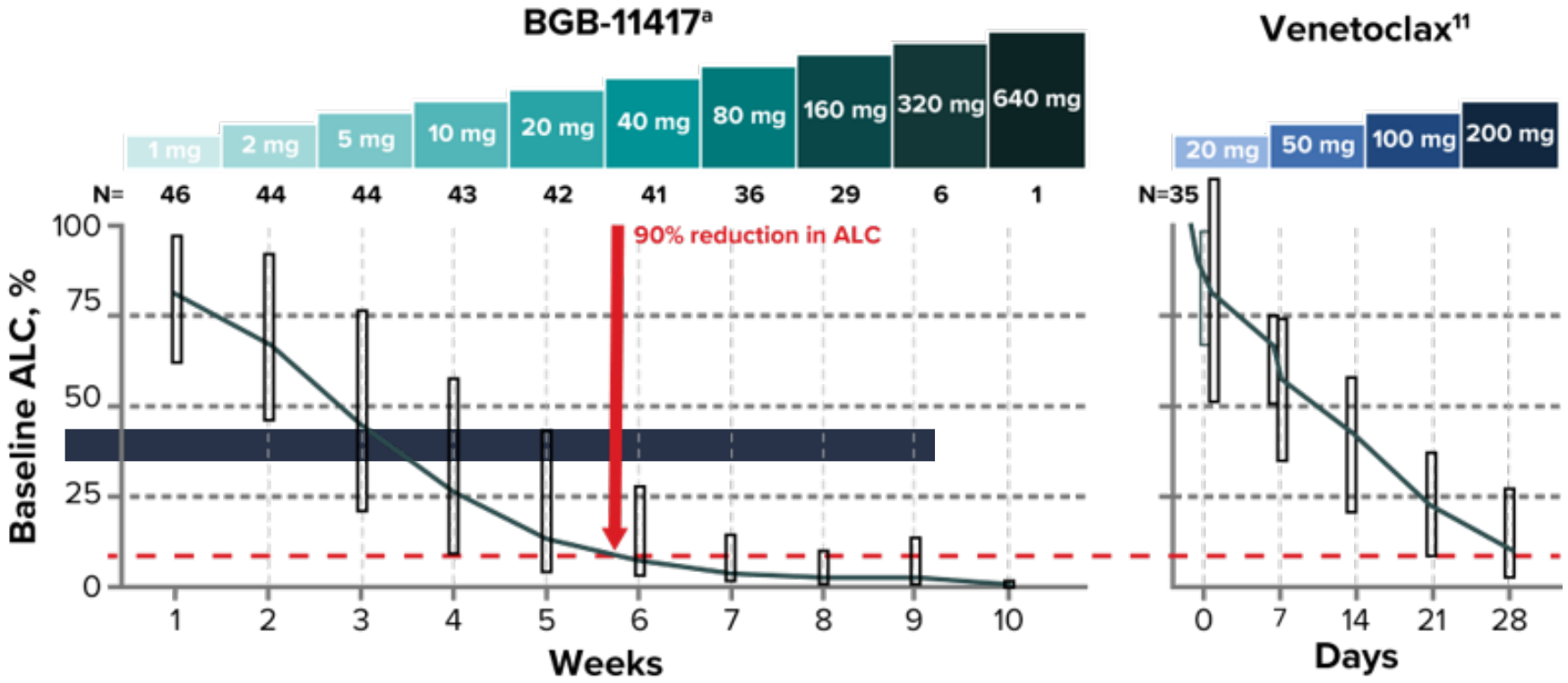
	Relative inhibition to BCL2				
	BCL-2	BCLxL	BCLw	MCL	AI
BGB-11417	1	1/2000	1/129,000	<1/714,000	<1/714,000
		1:6	1:9		
Venetoclax	1	1/325	1/13,700	<1/50,000	<1/50,000

Robust Pharmacodynamic Effect in Clinic Observed, Consistent with the Potency

Absolute lymphocyte count (ALC) dropped by ~90% after weekly ramp-up to 40 mg (BGB-11417 at 40 mg ≈ venetoclax at 200 mg [1:5])

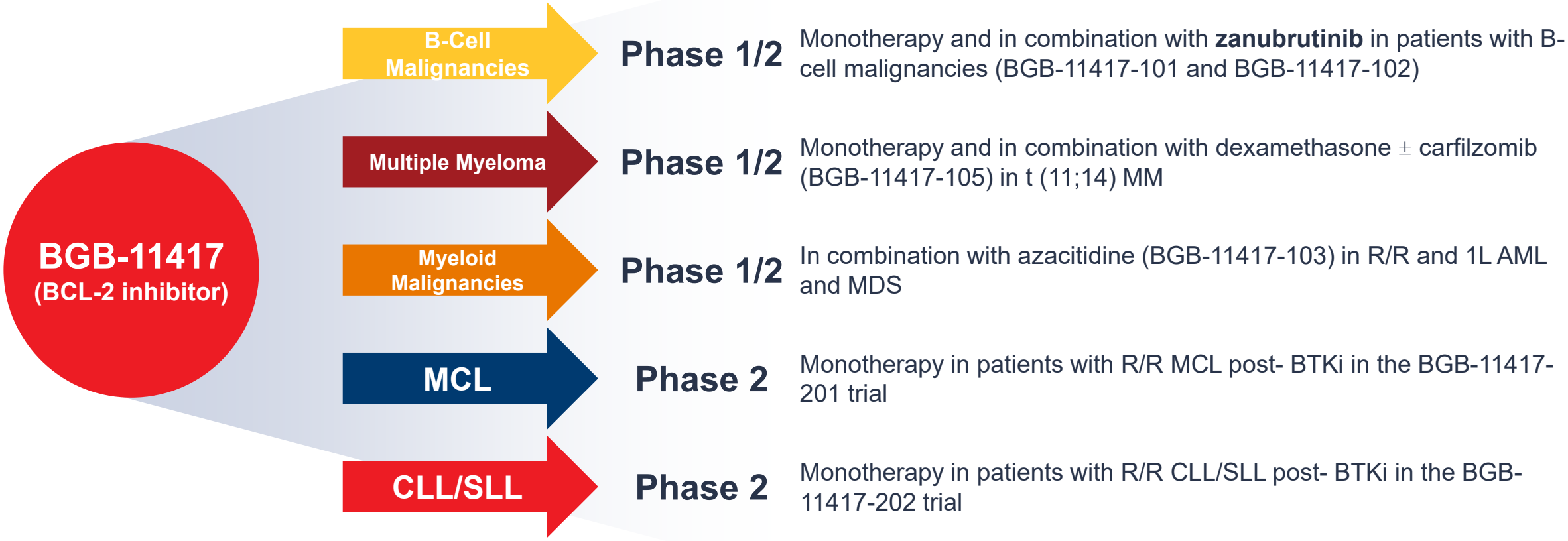
Equivalent ALC Reduction (%) by Dose After Weekly Ramp-Up

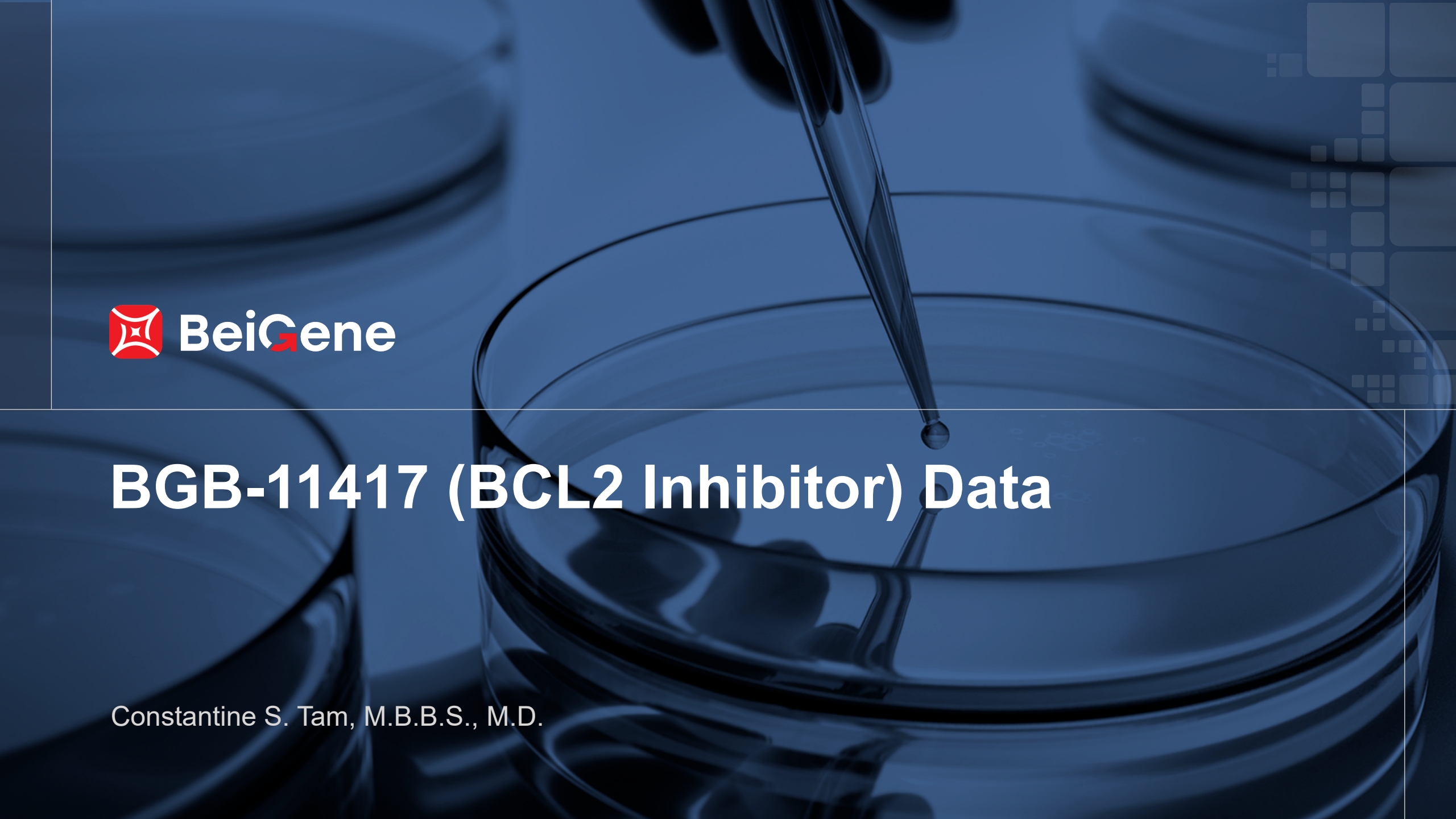
BGB-11417 dose	Venetoclax dose
1 - 2 mg	~20 mg
40 mg	~200 mg
80 mg	~400 mg



Only data from patients with an ALC >5x109/L at baseline are included. Box plots represent median and 10th-90th percentiles.
aMinimum ALC among 1 week of each dose level was used for calculation. N represents the number of patients who completed weekly dosing at dose level underneath. ALC data were pooled from both monotherapy (n=7) and combination therapy (n=39) cohorts because no difference was observed.

BGB-11417 Development Overview





BeiGene

BGB-11417 (BCL2 Inhibitor) Data

Constantine S. Tam, M.B.B.S., M.D.

Constantine (Con) Tam, M.B.B.S, M.D.

Head of Lymphoma Service at Alfred Health and Professor of Hematology at Monash University

- Dr. Tam is passionate about developing new treatments for blood cancers. He is the **global lead for zanubrutinib and oversaw its development from the first human dosed (in Melbourne)** to successful international licensing studies worldwide.
- Dr. Tam **designed and performed the first global study to combine ibrutinib and venetoclax**, publishing the results in the *New England Journal of Medicine* 5 years after inception.
- He has 259 peer-reviewed papers in *New England Journal of Medicine, Lancet, Journal of Clinical Oncology, Blood* and other top-tier journals. His work has been cited >18,000 times in the literature.
- Dr. Tam is Associate Editor for *Blood Advances*.
- He received his M.B.B.S.(Hons) and M.D. degrees from the University of Melbourne. After dual training in Hematology and Hematopathology, he completed his Leukemia Fellowship at MD Anderson Cancer Center. Prior to moving to the Alfred, **Dr. Tam served as Disease Group Lead for Low Grade Lymphoma and CLL at Peter MacCallum Cancer Centre & Royal Melbourne Hospital** for over 10 years.

ABSTRACT INFORMATION

Chan Y. Cheah,[1,2,3] Constantine S. Tam,[4,5] Masa Lasica,[6] Emma Verner,[7,8] Peter J. Browett,[9] Mary Ann Anderson,[10,11] James Hilger,[12] Yiqian Fang,[12] David Simpson, [12] and Stephen Opat[5,13]

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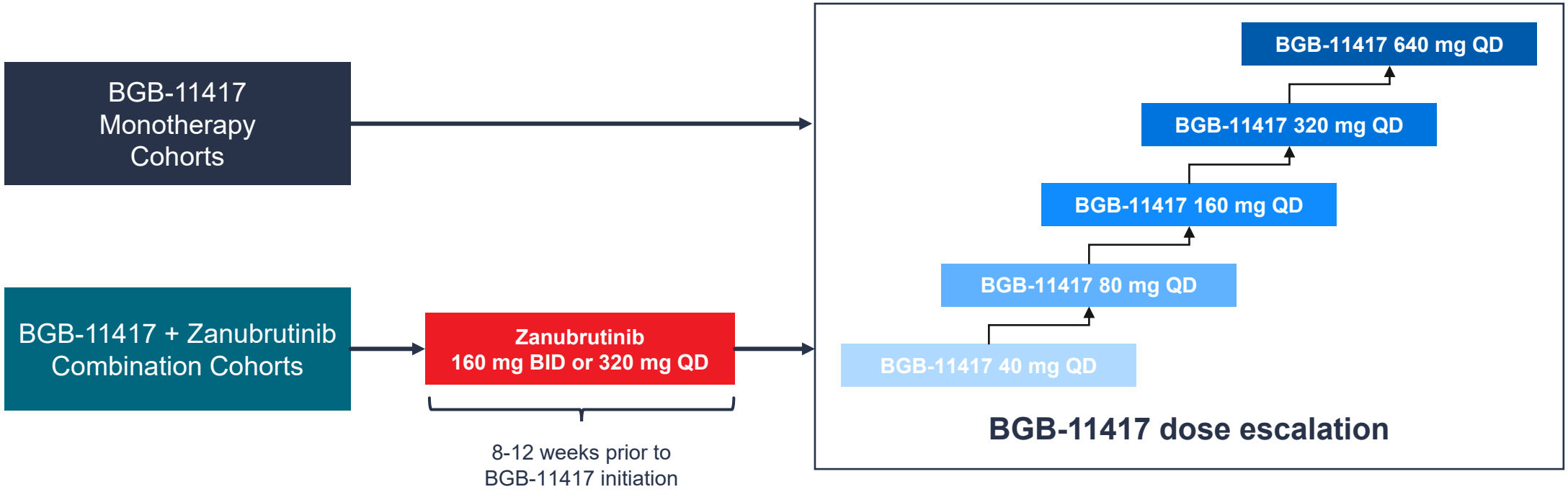
A Phase 1 Study With the Novel B-Cell Lymphoma 2 (Bcl-2) Inhibitor BGB-11417 as Monotherapy or in Combination With Zanubrutinib in Patients With CLL/SLL: Preliminary Data

Study Design

BGB-11417-101 – CLL/SLL Cohorts



- Patients received escalating doses of BGB-11417 with a ramp-up to the intended target dose to minimize risk of TLS
- In combination therapy cohorts, patients received zanubrutinib beginning 8-12 weeks before BGB-11417
- DLT for each cohort was evaluated by a Bayesian logistic regression model during dose ramp-up through day 21 at the intended dose
- AEs were reported per CTCAE v5.0
- MRD was assessed by a European Research Initiative on CLL flow cytometry assay

BID=twice daily, CLL=chronic lymphocytic leukemia, CTCAE=Common Terminology Criteria for Adverse Events, DLT=dose-limiting toxicity, MRD=minimal residual disease, QD=once daily, SLL=small lymphocytic lymphoma, TLS=tumor lysis syndrome,
Cheah C et al. Oral presentation presented at ASH 2022. Abstract 962

Patient Disposition and Dosing

BGB-11417-101 – CLL/SLL Cohorts

- 50 patients with CLL received treatment:
  - Monotherapy: N=6 (all R/R)
  - Combination: N=44 (22 R/R; 22 TN)

- Highest BGB-11417 doses received at data cutoff:
  - Monotherapy: Up to 160 mg
  - Combination:
    - R/R CLL: Up to 640 mg
    - TN CLL: Up to 320 mg
      - Data include 8 patients in zanubrutinib pre-treatment not yet dosed with BGB-11417

- Median follow-up:
  - Monotherapy: 11.5 months (range 8.5-18.3)
  - Combination: 5.8 months (range 0.2-10.5)

Data cutoff: May 15 2022
CLL=chronic lymphocytic leukemia, R/R=relapsed/refractory, TN=treatment naïve,
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Summary of Treatment-Emergent Adverse Events: Monotherapy

BGB-11417-101 – CLL/SLL Cohorts

- With monotherapy:
  - Cytopenias were the most common TEAEs (≥50%)
    - 33% were grade ≥3
- No patients discontinued treatment
- Only 1 high-risk pt on monotherapy had laboratory TLS that resolved with no intervention (overall laboratory TLS ≤2%)
- No patients experienced clinical TLS
- Diarrhea was mostly grade 1 and grade ≥3 was not seen

BGB-11417 monotherapy (R/R CLL; n=6)		
TEAEs (≥2 patients), n (%)	All grade	Grade ≥3
Thrombocytopenia†	4 (66.7)	2 (33.3)
Neutropenia*	3 (50)	2 (33.3)
Arthralgia	2 (33.3)	0
Contusion	2 (33.3)	0
Diarrhea	2 (33.3)	0
Musculoskeletal chest pain	2 (33.3)	0
Nausea	2 (33.3)	0
Oedema peripheral	2 (33.3)	0
Pyrexia	2 (33.3)	1 (16.7)

Data cutoff: May 15 2022
*includes neutrophil count decreased †includes platelet count decreased
CLL=chronic lymphocytic leukemia, TEAE=treatment emergent adverse event, TLS=tumor lysis syndrome,
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Summary of Treatment-Emergent Adverse Events: Combination

BGB-11417-101 – CLL/SLL Cohorts

- With combination therapy
  - Contusion, neutropenia, and low-grade gastrointestinal toxicity were the most common TEAEs (≥22.7%)
  - Neutropenia was the most common grade ≥3 TEAE (11.4%) with 5 patients

BGB-11417 + ZANU combination (CLL; n=44)		
TEAEs (≥3 patients), n (%)	All grade	Grade ≥3
Contusion	13 (29.5)	0
Neutropenia*	10 (22.7)	5 (11.4)
Diarrhea	10 (22.7)	0
Nausea	10 (22.7)	0
COVID-19	9 (20.5)	1 (2.27)
Fatigue	9 (20.5)	0
Headache	8 (18.2)	0
Constipation	7 (15.9)	0
Arthralgia	6 (13.6)	0
Petechiae	6 (13.6)	0
Back pain	4 (9.1)	0
Immunization reaction	4 (9.1)	0
Thrombocytopenia†	4 (9.1)	0
Abdominal pain	3 (6.8)	1 (2.27)
Epistaxis	3 (6.8)	0
Seasonal allergy	3 (6.8)	0

Data cutoff: May 15 2022
*includes neutrophil count decreased †includes platelet count decreased
CLL=chronic lymphocytic leukemia, TEAE=treatment emergent adverse event, TLS=tumor lysis syndrome,
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Please join us tomorrow – Monday, December 12 at 4:45pm CT

A Phase 1 Study With the Novel B-Cell Lymphoma 2 (Bcl-2) Inhibitor BGB-11417 as Monotherapy or in Combination With Zanubrutinib in Patients With CLL/SLL: Preliminary Data

Chan Y. Cheah,[1,2,3] Constantine S. Tam,[4,5] Masa Lasica,[6] Emma Verner,[7,8] Peter J. Browett,[9] Mary Ann Anderson,[10,11] James Hilger,[12] Yiqian Fang,[12] David Simpson, [12] and Stephen Opat[5],[13]

Accepted as: Oral Presentation
Date: 12/12/2022
Presentation time: 4:45pm CT
Session #: 642
Location: Ernest N. Morial Convention Center, Rooms 243-245

ABSTRACT INFORMATION

A Phase 1 Study With the Novel B-Cell Lymphoma 2 (Bcl-2) Inhibitor BGB-11417 as Monotherapy or in Combination With Zanubrutinib in Patients With Non-Hodgkin Lymphoma or Waldenström Macroglobulinemia: Preliminary Data

Jacob D. Soumerai[1], Masa Lasica[2*], Stephen Opat[3,4], Chan Y. Cheah[5,6,7], Henry Chan[8], Emma Verner[9,10*], Eva González Barca[11*], Alessandra Tedeschi[12*], James Hilger[13*], Yiqian Fang[13*], David Simpson[13*] and Constantine S. Tam[14,15*]

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[13]*BeiGene (Shanghai) Co., Ltd., Shanghai, China and BeiGene USA, Inc., San Mateo, CA*
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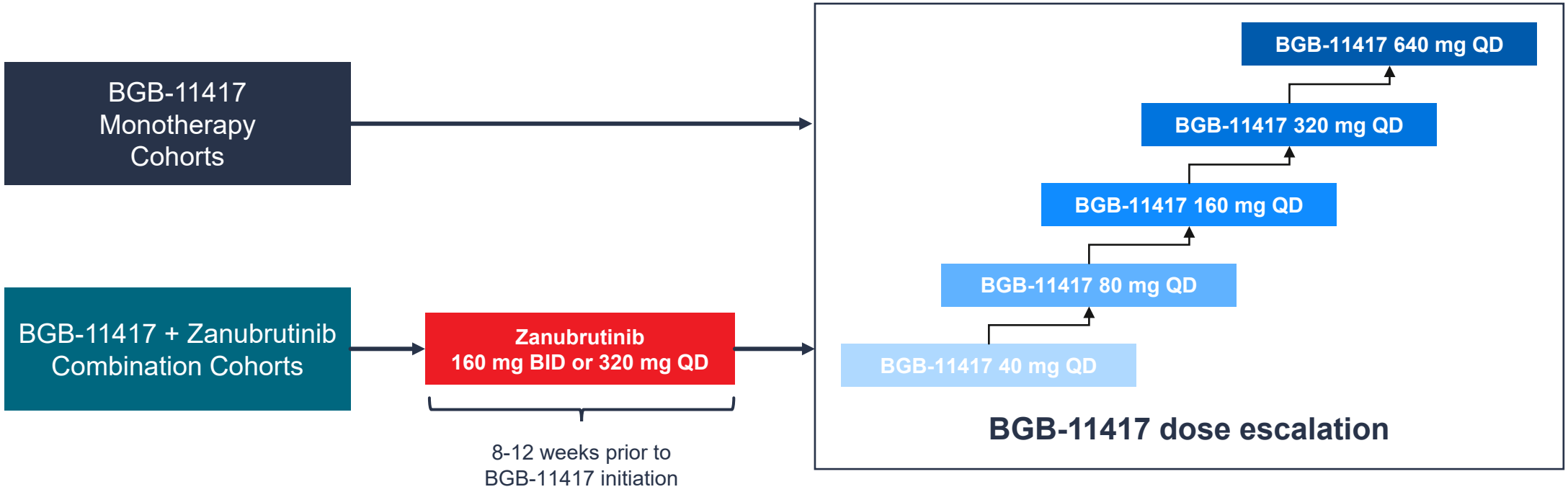
Study Design

BGB-11417-101 – NHL or WM Cohorts



- Patients in the monotherapy and combination cohorts received escalating doses of BGB-11417 with a ramp-up to the intended dose
- In combination cohorts, patients received zanubrutinib 8-12 weeks before BGB-11417
- DLT for each dose cohort was evaluated by a Bayesian logistic regression model during dose ramp-up through day 21 at the intended dose
- Responses were assessed per Lugano criteria
- AEs were reported per CTCAE v5.0, and TLS was assessed per Howard (2011) criteria

BID=twice daily, CLL=chronic lymphocytic leukemia, CTCAE=Common Terminology Criteria for Adverse Events, DLT=dose-limiting toxicity, QD=once daily, SLL=small lymphocytic lymphoma, TLS=tumor lysis syndrome,
Soumerai J et al. Poster presented at ASH 2022 Abstract 4201

Patient Disposition and Dosing

BGB-11417-101 – NHL or WM Cohorts

- 45 patients with NHL, WM, or MCL received BGB-11417:
  - Monotherapy: N=34
    - NHL: n=28 (n=18 DLBCL; n=6 FL; n=4 MZL)
    - WM: n=6
  - Combination: N=11 (all MCL)
- Monotherapy patients received BGB-11417 at doses ≤640 mg
- Combination patients received zanubrutinib and 9 (82%) received BGB-11417 at doses ≤160 mg
  - Data include 2 patients still in zanubrutinib pre-treatment
- Dose escalation to 640 mg was completed for NHL monotherapy; all planned doses were tested, with no MTD reached
  - Dose escalation is ongoing for monotherapy in WM and combination therapy in MCL cohorts
- Median follow-up:
  - Monotherapy: 6.5 months (range 0.4-25.3)
  - Combination: 4.8 months (range 0.4-8.9)

Data cutoff: May 15 2022
DLBCL=diffuse large B-cell lymphoma, FL=follicular lymphoma, MCL=mantle cell lymphoma, MTD=maximum tolerated dose, MZL=marginal zone lymphoma, NHL=non-Hodgkin's lymphoma, MCL=mantle cell lymphoma, WM=Waldenström's macroglobulinemia,
Soumerai J et al. Poster presented at ASH 2022 Abstract 4201

Summary of Treatment-Emergent Adverse Events: Monotherapy

BGB-11417-101 – NHL or WM Cohorts

- For monotherapy:
  - The most common TEAEs (≥20%) were nausea (38%), fatigue (24%), constipation, diarrhea and dizziness (21% each)
  - The most common grade ≥3 TEAE was neutropenia (12%).
- Twenty-five monotherapy patients discontinued treatment:
  - 22 PD; 1 AE; 2 other reasons
- No TEAEs leading to death and no TLS were reported to date

BGB-11417 monotherapy (R/R NHL + WM; n=34)		
TEAEs (≥3 patients), n (%)	**All grade**	**Grade ≥3**
Nausea	13 (38.2)	0
Fatigue	8 (23.5)	0
Constipation	7 (20.6)	0
Diarrhea	7 (20.6)	0
Dizziness	7 (20.6)	0
Fall	6 (17.6)	2 (5.9)
Headache	6 (17.6)	0
Neutropenia*	5 (14.7)	4 (11.8)
Pyrexia	5 (14.7)	0
Abdominal pain	4 (11.8)	2 (5.9)
Anemia	4 (11.8)	1 (2.9)
Urinary tract infection	4 (11.8)	0
Vomiting	4 (11.8)	0
Arthralgia	3 (8.8)	1 (2.9)
AST increased	3 (8.8)	1 (2.9)
Back pain	3 (8.8)	1 (2.9)
Dyspnea	3 (8.8)	0
Hypotension	3 (8.8)	0
Lethargy	3 (8.8)	0
Oedema peripheral	3 (8.8)	0
Cough	3 (8.8)	0

Data cutoff: May 15 2022
*includes neutrophil count decreased
AE=adverse event, AST=aspartate aminotransferase, NHL=non-Hodgkin's lymphoma, PD=progressive disease, R/R=relapsed/refractory, TEAE=treatment emergent adverse event, TLS=tumor lysis syndrome, WM=Waldenström's macroglobulinemia,
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Summary of Treatment-Emergent Adverse Events: Combination

BGB-11417-101 – NHL or WM Cohorts

- For combination therapy:
  - The most common TEAEs (≥20%) were contusion (27.3%) and neutropenia (27.3%); grade ≥3 AEs were infrequent
- 2 patients discontinued treatment (both PD)

BGB-11417+ZANU combination (R/R MCL; n=11)*		
TEAEs (≥2 patients), n (%)	**All grade**	**Grade ≥3**
Contusion	3 (27.3)	0
Neutropenia†	3 (27.3)	1 (9.1)
Herpes zoster	2 (18.2)	0
Lethargy	2 (18.2)	0
Nausea	2 (18.2)	0
Thrombocytopenia‡	2 (18.2)	1 (9.1)

Data cutoff: May 15 2022
*Two patients had not yet received BGB-11417 at the time of analysis. †includes neutrophil count decreased ‡includes platelet count decreased
AE=adverse event, AST=aspartate aminotransferase, NHL=non-Hodgkin's lymphoma, PD=progressive disease, R/R=relapsed/refractory, TEAE=treatment emergent adverse event, TLS=tumor lysis syndrome, WM=Waldenström's macroglobulinemia,
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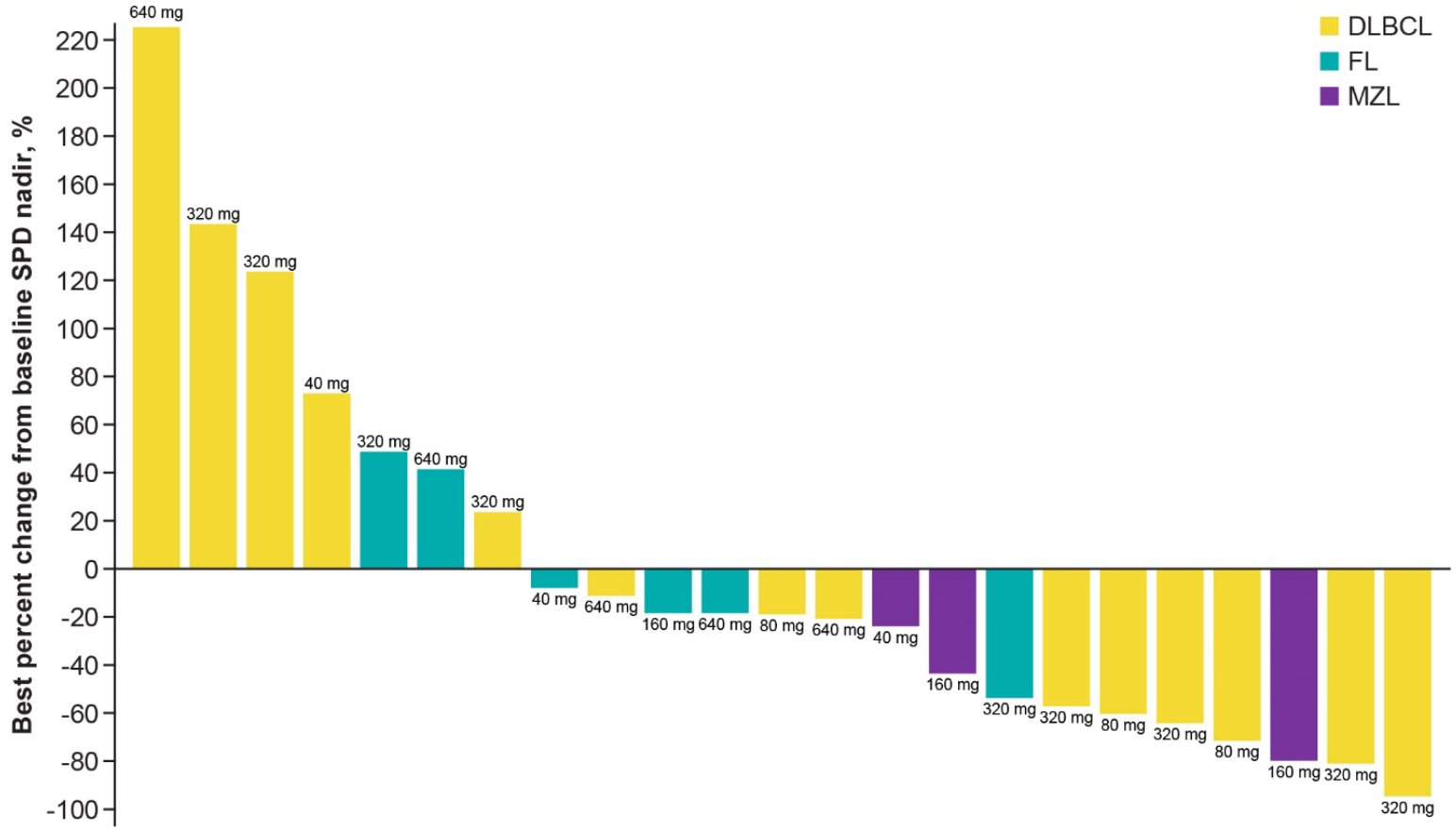
Percent Change From Baseline in SPD Among Efficacy Evaluable Patients With NHL

BGB-11417-101 – NHL or WM Cohorts



- Notable reductions in the SPD were seen among patients with DLBCL, FL, and MZL

Data cutoff: May 15 2022
WM and MCL are treated in separate cohorts and are not included in this figure
DLBCL=diffuse large B-cell lymphoma, FL=follicular lymphoma, MCL=mantle cell lymphoma, MZL=marginal zone lymphoma, SPD=sum of the products of diameters, FL=follicular lymphoma,
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Anti-Tumor Response

BGB-11417-101 – NHL or WM Cohorts

- NHL cohorts:
  - 23 patients reached the first response assessment time point, but most were treated below the recommended phase 2 dose
    - Of these patients, 3 responded (n=2 DLBCL, n=1 MZL) including 1 complete response (DLBCL)
- In the MCL combination cohort:
  - 6 of 11 (55%) patients responded
- In the monotherapy WM cohort:
  - 1 of 4 evaluable patients exhibited minor response at the first dose level tested (80 mg)
  - Hemoglobin count increases of more than 20 g/L were seen in 3 of 6 treated patients and all remain on treatment

Data cutoff: May 15 2022
DLBCL=diffuse large B-cell lymphoma, NHL=non-Hodgkin's lymphoma, MCL=mantle cell lymphoma, MZL=marginal zone lymphoma, WM=Waldenström's macroglobulinemia,
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Author Conclusions

BGB-11417-101 – NHL or WM Cohorts

- These initial data show an encouraging safety profile and preliminary evidence of efficacy for BGB-11417 in NHL, MCL, and WM cohorts
- No MTD was reached even at the highest dose level of 640 mg QD
- All low-grade TEAEs and grade ≥3 neutropenia were manageable
- The response data includes NHL patients mostly treated at doses below the RP2D; longer follow-up of BGB-11417 monotherapy and combination therapy at the RP2D is needed
- Monotherapy MCL data are forthcoming

Data cutoff: May 15 2022
NHL=non-Hodgkin's lymphoma, MCL=mantle cell lymphoma, QD=once daily, RP2D=recommended phase 2 dose, TEAE=treatment emergent adverse event, WM=Waldenström's macroglobulinemia,
Cheah C et al. Oral presentation presented at ASH 2022. Abstract 962

Preliminary Safety and Efficacy of BGB-11417, a Novel Bcl-2 Inhibitor, in Combination With Azacitidine in Patients With Acute Myeloid Leukemia

Jake Shortt,[1] Pau Montesinos,[2] Shuh Ying Tan,[3] Teng Fong Ng,[4] Chun Yew Fong,[5] Paul Cannell,[6] Kirsty Marshall,[7] Sophie Leitch,[8] Peter Tan,[9] Sundra Ramanathan,[10] Robin Gasiorowski,[11] Douglas Lenton,[12] Tse-Chieh Teh,[13] José Antonio Pérez-Simón,[14] Carolyn Grove,15 Xiaojun Huang,[16] Courtney DiNardo,[17] Katherine Naidu,[18] Joseph Pariseau,[18] Si Cheng,[18] Yu Liu,[18] Melannie Co,[18] Wai Y. Chan,[18] Haiyi Guo,[18] and Andrew H. Wei[19]

[1]Monash Health and Monash University, Clayton, Victoria, Australia; [2]Hospital Politecnico Universitario La Fe, Valencia, Spain; [3]St Vincent's Hospital Melbourne, Fitzroy, Victoria, Australia; [4]Gold Coast University Hospital, Southport, Queensland, Australia; [5]Austin Health, Heidelberg, Victoria, Australia; [6]Fiona Stanley Hospital, Murdoch, Western Australia, Australia; [7]Middlemore Hospital, Auckland, New Zealand; [8]North Shore Hospital, Auckland, New Zealand; [9]One Clinical Research, Nedlands, Western Australia, Australia; [10]The Saint George Hospital-Kogarah, Kogarah, New South Wales, Australia; [11]Concord Repatriation General Hospital, Concord West, New South Wales, Australia; [12]Orange Health Service (Central West Cancer Care Centre), Orange, New South Wales, Australia; [13]Department of Clinical Haematology, The Alfred Hospital, Prahran, Victoria, Australia; [14]Hospital Universitario Virgen del Rocio, Instituto de Biomedicina de Sevilla (IBS/CISC), Universidad de Sevilla, Spain; [15]Linear Clinical Research, PathWest & Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia; [16]Peking University People's Hospital, Beijing, China; [17]University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [18]BeiGene (Shanghai) Co., Ltd., Shanghai, China and BeiGene USA, Inc., San Mateo, CA, USA; and [19]Department of Clinical Haematology, Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Victoria, Australia

64th ASH Annual Meeting and Exposition,
December 10-13, 2022 **Abstract 1443**

Study Design

BGB-11417-103 – AML cohort

PHASE 1

Study Identifier: BGB-11417-103, NCT04771130

Primary Endpoint: Safety and tolerability, RP2D of combination in AML (parts 1 and 2), CR + CRh rate; (part 3)
Key Secondary Endpoints: PK, biomarkers

KEY ELIGIBILITY CRITERIA

- Aged ≥18 years
- AML (non-APL)
- TN unfit for intensive chemotherapy
- R/R with no prior Bcl-2 inhibitor or azacitidine exposure
- ECOG PS 0-2
- Not receiving warfarin; moderate or strong CYP3A4 inhibitor or inducer within 5 half-lives

PART 1 DOSE ESCALATION → **PART 2 SAFETY EXPANSION** → **PART 3 EFFICACY EXPANSION**

BGB-11417 (10 days or 28 days in 28-day cycle with 4-day ramp up in cycle 1 starting at 1/8 of the target dose[a])
+
Azacitidine (75 mg/m^2 for 7 days SC or IV)

BGB-11417 dose	Part 1	Part 2
40 mg x 10 days	3-6 patients	~10 patients
80 mg x 10 days	3-6 patients	~10 patients
160 mg x 10 days	3-6 patients	~10 patients
160 mg x 28 days	3-6 patients	~10 patients

RP2D

Part 3
~20 patients

- Response assessments based on European LeukemiaNet 2017 Response Criteria with assessment of hematologic improvement1,2 were performed every 3 cycles starting at the end of cycle 1
- For patients not in remission, an additional response assessment was performed at the end of cycle 2
- MRD status was assessed by multiparameter flow cytometry3 at the end of cycles 1 and 4, and at the end of cycle 2 if additional response assessment was performed

aPatients were hospitalized during the ramp-up period for TLS monitoring.4
Safety monitoring committee reviews available patient safety and preliminary efficacy data to determine dose escalation in part 1, dose expansion to part 2, and the final RP2D to start part 3.
1. Bloomfield CD, et al. Blood Rev 2018;32(5):416-425 2. Döhner H, et al. Blood 2017;129(4):424-447 3. Schuurhuis GJ, et al. Blood 2018;131(12):1275-1291 4. Howard SC, et al. N Engl J Med 2011;364(19):1844-1854. Erratum in: N Engl J Med 2018;379(11):1094
AML=acute myeloid leukemia, APL=acute promyelocytic leukemia, CR=complete response, CRh=complete response with partial hematologic recovery, ECOG=Eastern Cooperative Oncology Group, IV=intravenous, PS=performance status, PK=pharmacokinetics, R/R=relapsed/refractory, RP2D=recommended phase 2 dose, SC=subcutaneous,
Shortt J et al. Poster presented at ASH 2022 Abstract 1443. This study is registered at ClinicalTrials.gov (NCT04771130).

Baseline Characteristics

BGB-11417-103 – AML cohort

Characteristics, n (%)	**TN (n=31)**	**R/R (n=26)**	**All (N=57)**
Median age (range), years	77 (64-91)	64 (29-80)	71 (29-91)
Male	19 (61)	16 (62)	35 (61)
AML type			
De novo	26 (84)	23 (88)	49 (86)
AML risk stratifications[a]			
Intermediate	11 (35)	8 (31)	19 (33)
Adverse	11 (35)	13 (50)	24 (42)
Bone marrow blast count			
≥30 to <50%	11 (35)	3 (12)	14 (25)
≥50%	12 (39)	11 (42)	23 (40)

Characteristics, n (%)	**TN (n=31)**	**R/R (n=26)**	**All (N=57)**
Most common genetic abnormalities			
inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*	3 (10)	7 (27)	10 (18)
NPM1	4 (13)	5 (19)	9 (16)
-7 or del(7q)	5 (16)	3 (12)	8 (14)
Complex karyotype or monosomal karyotype	5 (16)	3 (12)	8 (14)
-5 or del(5q)	5 (16)	2 (8)	7 (12)
IDH1	2 (6)	5 (19)	7 (12)
RUNX1	2 (6)	4 (15)	6 (11)
FLT3[b]	4 (13)	2 (8)	6 (11)
IDH2[c]	1 (3)	5 (19)	6 (11)
TP53 aneuploidy	4 (13)	1 (4)	5 (9)
t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*	3 (10)	1 (4)	4 (7)

Data cutoff: September 5, 2022
aBased on 2017 ELN risk stratifications by genetics. bFLT3-ITD (low or high allelic ratio), none FLT3-TKD. cIncludes R140 and R172 mutations.
AML=acute myeloid leukemia, ELN=European LeukemiaNet, R/R=relapsed/refractory, TN=treatment naïve,
Shortt J et al. Poster presented at ASH 2022 Abstract 1443`

Summary of TEAEs

BGB-11417-103 – AML cohort

TEAEs, n (%)	**Total (N=57)**
Any TEAE	57 (100)
Grade ≥3	53 (93)
Serious	46 (81)
Leading to death	6 (11)
Death within 30 days of first dose	1 (2)
Death within 60 days of first dose	3 (5)
Leading to discontinuation	
BGB-11417	10 (18)
Azacitidine	11 (19)
Leading to reduction	
BGB-11417	6 (11)
Azacitidine	9 (16)
Leading to cycle delays	
BGB-11417	37 (65)
Azacitidine	37 (65)

Data cutoff: September 5, 2022
AML=acute myeloid leukemia, COPD=chronic obstructive pulmonary disease, R/R=relapsed/refractory, TEAE=treatment emergent adverse event, TN=treatment naïve,
Shortt J et al. Poster presented at ASH 2022 Abstract 1443`

Dose-Limiting Toxicities and Tumor Lysis Syndrome

BGB-11417-103 – AML cohort

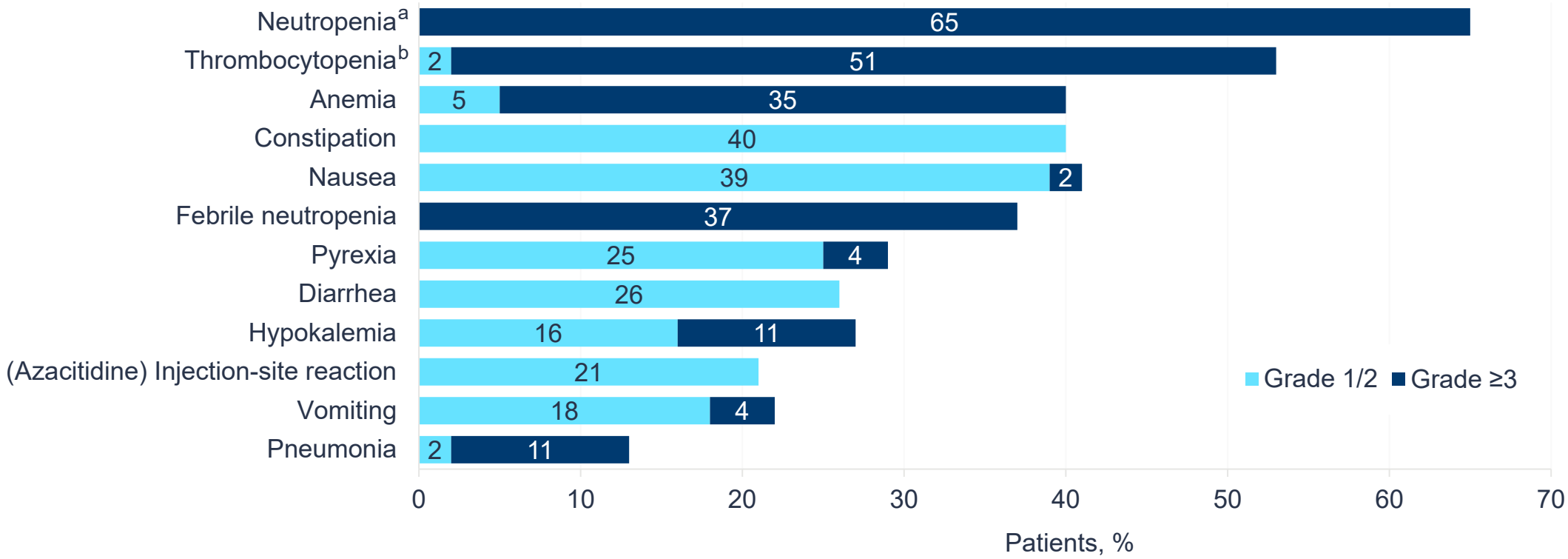
	BGB-11417				
	40 mg x 10 days	80 mg x 10 days	160 mg x 10 days	160 mg x 28 days	Total
DLT evaluable[a], n (%)	**(n=14)**	**(n=15)**	**(n=15)**	**(n=6)**	**(n=50)**
DLT	0	2 (13)	0	0	2 (4)
Hematologic	0	2 (13)	0	0	2 (4)
Grade 4 neutropenia	0	1 (7)	0	0	1 (2)
Grade 4 thrombocytopenia	0	2 (13)	0	0	2 (4)
Nonhematologic (grade ≥3)	0	0	0	0	0

- DLT (grade 4 neutropenia and thrombocytopenia lasting beyond day 42) occurred in 2 patients in the 80 mg x 10 days cohort. No new DLTs were observed with higher doses
- No clinical TLS was observed
- Laboratory TLS occurred in a patient treated with 160 mg x 10 days (assessed based on Howard criteria6)
  - This patient had pre-existing history of chronic kidney disease. He was managed successfully as an outpatient and fully recovered after 4 days

Data cutoff: September 5, 2022
aBased on DLT evaluable set, which includes patients who completed the DLT observation window and received ≥80% of the intended cumulative dose.
DLT=dose-limiting toxicity, TLS=tumor lysis syndrome
Shortt J et al. Poster presented at ASH 2022 Abstract 1443`

Most Common TEAEs (≥20% for All Grades or ≥10% for Grade ≥3)

BGB-11417-103 – AML



- The most common TEAEs were neutropenia, thrombocytopenia and anemia, and the most common non-hematologic TEAEs were nausea and constipation (majority were grade1/2)

Data cutoff: September 5, 2022
aNeutropenia includes neutropenia and decreased neutrophil count. bThrombocytopenia includes thrombocytopenia and decreased platelet count.
TEAE=treatment emergent adverse event,
Shortt J et al. Poster presented at ASH 2022 Abstract 1443`

Summary of Complete Responses

BGB-11417-103 – AML

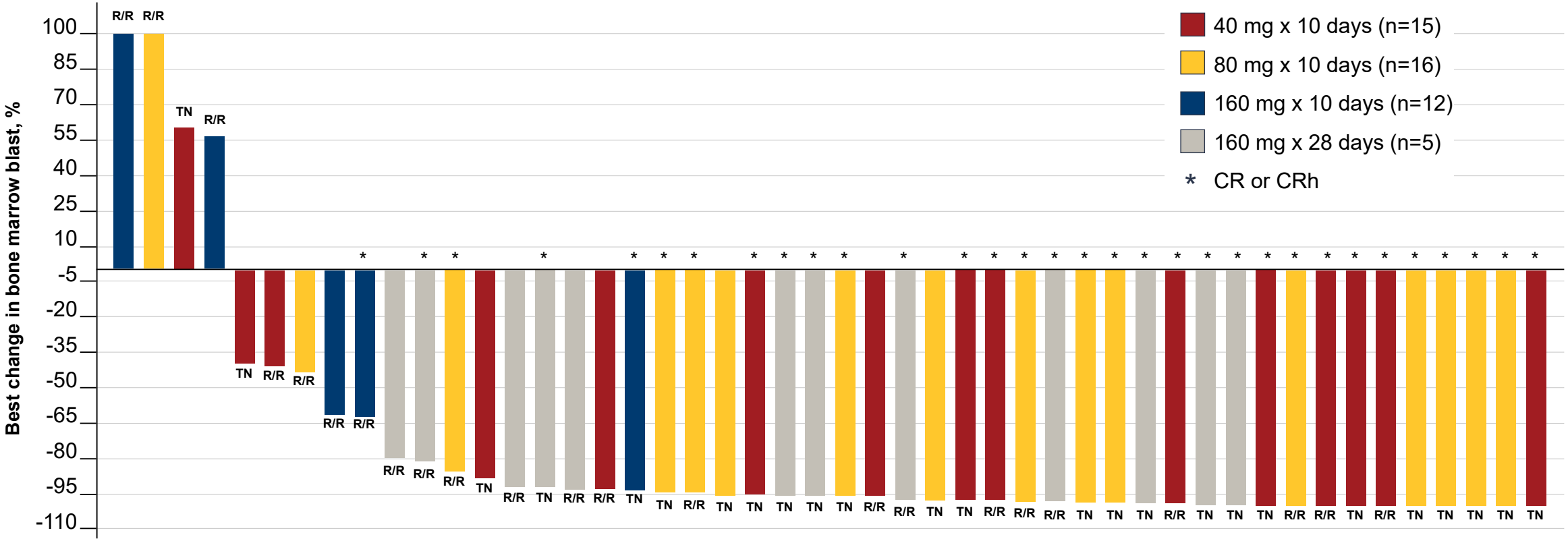
Response	40 mg x 10 days		80 mg x 10 days		160 mg x 10 days		160 mg x 28 days		Total	
	TN (n=9)	R/R (n=7)	TN (n=11)	R/R (n=6)	TN (n=8)	R/R (n=8)	TN (n=3)	R/R (n=5)	TN (n=31)	R/R (n=26)
CR+CRh,[a] n (%)	5 (56)	4 (57)	8 (73)	4 (67)	6 (75)	3 (38)	1 (33)	2 (40)	20 (65)	13 (50)
CR+CRh after 1 cycle	4 (44)	1 (14)	5 (45)	1 (17)	5 (63)	1 (13)	1 (33)	2 (40)	15 (48)	5 (19)
CR+CRi, n (%)	5 (56)	3 (43)	8 (73)	4 (67)	6 (75)	3 (38)	1 (33)	2 (40)	20 (65)	12 (46)
CR	4 (44)	2 (29)	8 (73)	3 (50)	3 (38)	1 (13)	1 (33)	1 (20)	16 (52)	7 (27)
Median time to CR, months	1.3	3.2	1.8	3.8	1.2	1.9	1.2	1.1	1.3	3.8
Median BGB-11417 treatment duration, (range), months	4.9 (0.3-10.6)	1.7 (1.3-6.2)	7.8 (0.3-15.2)	7.3 (0.4-15.4)	3.3 (0.3-9.9)	2.3 (0.1-9.7)	1.4 (0.0-2.7)	2.3 (0.9-4.1)	3.7 (0.0-15.2)	2.6 (0.1-15.4)

- CR+CRh was achieved in 65% of TN and 50% of R/R patients
  - Most CR+CRh in TN AML (15 of 20) was achieved by the end of cycle 1

Data cutoff: September 5, 2022
aCRh was defined by Bloomfield et al.7
Response assessments based on ELN 2017 Response Criteria with assessment of hematologic improvement (part 3).7,8
Number of patients who did not have a posttreatment response assessment: in TN 40 mg and 80 mg (n=1 each), in TN 160 mg x 10 days and x 28 days (n=2 each), and in R/R 160mg x 10 days (n=1).
CR=complete response, CRh=complete response with partial hematologic recovery, R/R=relapsed/refractory, TN=treatment naïve,
Shortt J et al. Poster presented at ASH 2022 Abstract 1443`

Best Change From Baseline in Bone Marrow Blasts

BGB-11417-103 – AML



- Twenty-seven patients met CR+CRh with evaluable flow cytometry MRD results, and 13 (48%) of the 27 achieved MRD negativity (malignant AML <0.1% per ELN 2018[1])

Data cutoff: September 5, 2022
AML=acute myeloid leukemia, CR=complete response, CRh=complete response with partial hematologic recovery, ELN=European LeukemiaNet, MRD=minimal residual disease, R/R=relapsed/refractory, TN=treatment naïve
1. Schuurhuis GJ, et al. Blood 2018;131(12):1275-1291
Shortt J et al. Poster presented at ASH 2022 Abstract 1443`

Author Conclusions

BGB-11417-103 – AML

- BGB-11417 (40, 80, 160 mg) plus azacitidine was generally well tolerated in patients with AML
  - DLTs (grade 4 neutropenia/ thrombocytopenia) only occurred in the 80 mg cohort; no new DLTs occurred with further dose escalation
  - Neutropenia (65%) was the most common grade ≥3 TEAE, manageable with dose modifications and supportive care
  - No dose-dependent toxicities were observed
  - Maximum tolerated dose was not reached
- The combination was effective in both TN and R/R settings at the four dose levels tested
  - CR/CRh was achieved in 65% TN and 50% R/R patients
- Efficacy analysis of molecular subgroups, safety expansion, and evaluation of higher doses of BGB-11417 are ongoing; inclusion of patients with AML who failed hypomethylating agents is also planned

Data cutoff: September 5, 2022
AML=acute myeloid leukemia, CR=complete response, CRh=complete response with partial hematologic recovery, DLT=dose-limiting toxicity, R/R=relapsed/refractory, TEAE=treatment emergent adverse event, TN=treatment naïve,
Shortt J et al. Poster presented at ASH 2022 Abstract 1443`

Preliminary Safety of a Bcl-2 Inhibitor, BGB-11417, in Patients With Relapsed/Refractory Multiple Myeloma Harboring t(11,14): A Nonrandomized, Open-Label, Phase 1b/2 Study

Hang Quach,[1] Rajeev Rajagopal,[2] Andrew Spencer,[3] Michael Low,[4] Dickran Kazandijan,[5] Rocco Crescenzo,[6] Chenmu Du,[6] Sheel Patel,[6] Vaibhav Mundra,[6] Huan Cheng,[6] and Binod Dhakal[7]

[1]St. Vincents Hospital Melbourne, University of Melbourne, Melbourne, Australia; [2]Middlemore Hospital, Auckland, New Zealand; [3]The Alfred Hospital, Melbourne, Australia; [4]Monash Health, Melbourne, Australia; [5]Sylvester Comprehensive Cancer Center, Miami, Florida, USA; [6]BeiGene USA, Inc., San Mateo, CA, USA; and [7]Medical College of Milwaukee, Wisconsin, USA

December 11, 2022
653. Myeloma and Plasma Cell Dyscrasias: Prospective Therapeutic Trials: Poster II

64th ASH Annual Meeting and Exposition,
December 10-13, 2022 **Abstract 3235**

Study Design

BGB-11417-105 – MM

PHASE 1

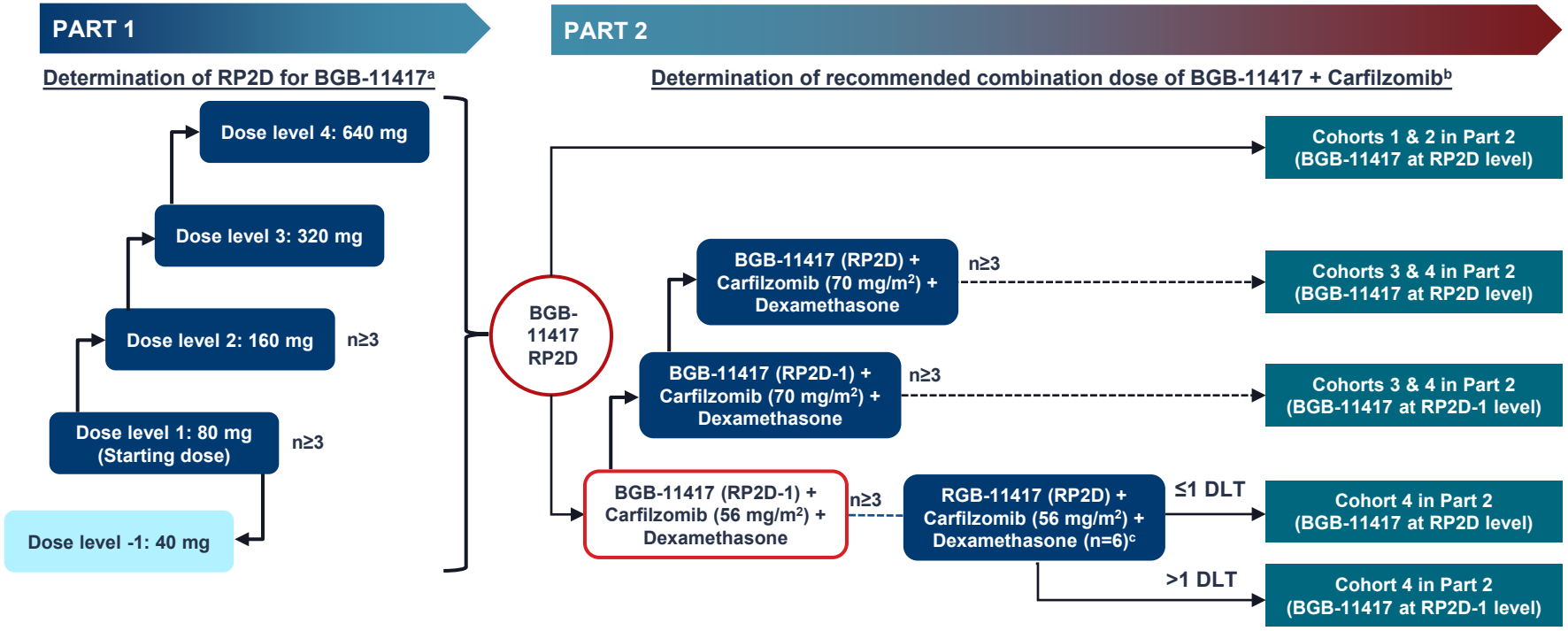
Study Identifier: BGB-11417-105, NCT04973605

Primary Endpoint: Safety, tolerability, and RP2D of BGB-11417 in combination with dexamethasone with or without carfilzomib, MTD for BGB-11417 in combination with dexamethasone

Key Secondary Endpoints: PK of BGB-11417 in combination with dexamethasone with or without carfilzomib, ORR of BGB-11417 in combination with dexamethasone with or without carfilzomib; PK of dexamethasone in combination with BGB-11417

KEY ELIGIBILITY CRITERIA

- Confirmed diagnosis of MM (must have an M-component in serum and/or urine)
- ECOG PS 0-2
- Measurable disease[c]
- Documented relapsed or progressive MM on or after any regimen or who are refractory to the most recent line of therapy
- Positivity for t(11;14) by FISH



Dashed arrow indicated the dose combination of BGB-11417 + carfilzomib is selected as the combination MTD or MAD.
aBGB-11417 + dexamethasone (40 mg weekly); dose escalation guided by mTPI-2: target toxicity probability = 0.2, EI = (0.15, 0.25); maximum dose sample size = 18. bBGB-11417 + carfilzomib (56 mg/m2 or 70 mg/m2 weekly + dexamethasone (40 mg weekly); dose escalation guided by mTPI-2: target toxicity probability = 0.25, EI = (0.2, 0.3); maximum dose sample size = 18 + 6 for BGB-11417 RP2D + carfilzomib 56 mg/m2 + dexamethasone. cCan open as soon as the dose combination of BGB-11417 (R2PD-1) + carfilzomib (70 mg/m2) + dexamethasone is suggested to be eliminated and data of BGB-11417 (R2PD-1) + carfilzomib (56 mg/m2) + dexamethasone allow for further dose escalation per mTPI-2 decision table. c M-spike ≥ 500mg/dL, or ii. Urine protein M-spike of ≥ 200 mg/day, or iii. Serum free light chains ≥ 10 mg/dL, and an abnormal κ:λ ratio
DLT=dose-limiting toxicity, ECOG=Eastern Cooperative Oncology Group, FISH=fluorescence in situ hybridization, MAD=maximum administered dose, MM=multiple myeloma, MTD=maximum tolerated dose, ORR=overall response rate, PK=pharmacokinetics, PS=performance status, RP2D=recommended phase 2 dose,
Quach H et al. Poster presented at ASH 2022 Abstract 3235 This study is registered at ClinicalTrials.gov (NCT04973605).

Treatment-Emergent AEs Occurring in ≥2 Patients

BGB-11417-105 – MM

AEs, n (%)	BGB-11417 (80mg) (n=3)	BGB-11417 (160mg) (n=3)	BGB-11417 (320mg) (n=3)	BGB-11417 (640mg) (n=3)	All Patients (N=12)
Insomnia	1 (33)	3 (100)	2 (67)	0	6 (50)
COVID-19	0	1 (33)	1 (33)	1 (33)	3 (25)
Fatigue	1 (33)	0	2 (67)	0	3 (25)
Alopecia	0	1 (33)	0	1 (33)	2 (17)
Arthralgia	1 (33)	0	1 (33)	0	2 (17)
Back pain	0	1 (33)	1 (33)	0	2 (17)
Dyspnea	0	0	2 (67)	0	2 (17)
Nausea	1 (33)	1 (33)	0	0	2 (17)

- One patient had grade 2 neutropenia, which did not lead to dose modifications or discontinuation

Data cutoff: 16 September 2022.
AE=adverse event, COVID=coronavirus disease,
Quach H et al. Poster presented at ASH 2022 Abstract 3235

Disease Response by Investigator

BGB-11417-105 – MM

AEs, n (%)	BGB-11417 (80mg) (n=3)	BGB-11417 (160mg) (n=3)	BGB-11417 (320mg) (n=3)	BGB-11417 (640mg) (n=3)	All Patients (N=12)
Best overall response, n (%)					
sCR	0	0	0	0	0
CR	0	1 (33)	0	0	1 (8)
VGPR	0	0	0	0	0
PR	0	1 (33)	2 (67)	1 (33)	4 (33)
MR	0	0	0	1 (33)	1 (8)
SD	2 (67)	1 (33)	1 (33)	0	4 (33)
PD	1 (33)	0	0	0	1 (8)
Ongoing without baseline tumor assessment	0	0	0	1 (33)	1 (8)
ORR, n (%)	0	2 (68)	2 (67)	1 (33)	5 (42)
(95% CI)[a]	(0-71)	(9-99)	(9-99)	(1-91)	(15-72)
VGPR or BRR, n (%)	0	1 (33)	0	0	1 (8)
(95% CI)[a]	(0-71)	(1-91)	(0-71)	(0-71)	(0-39)

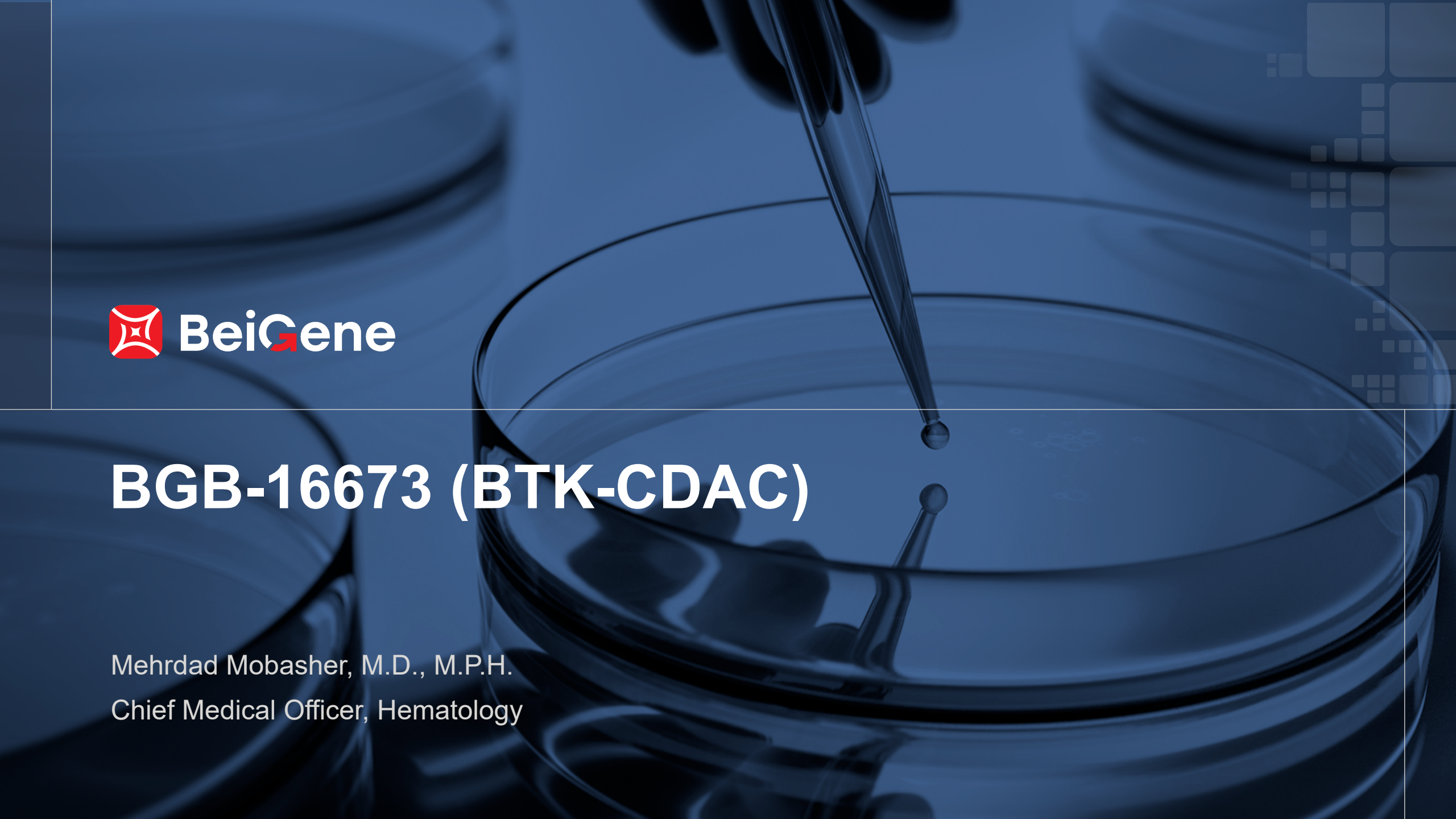
Data cutoff: 16 September 2022.
aThe 95% CI was estimated using the Clopper-Pearson method
BRR=better response rate, CI=confidence interval, CR=complete response, MR=minor response, ORR=overall response rate, PD=progressive disease, PR=partial response, sCR=stringent complete response, SD=stable disease, VGPR=very good partial response
Quach H et al. Poster presented at ASH 2022 Abstract 3235

Author Conclusions

BGB-11417-105 – MM

- These early phase 1 results suggest that BGB-11417 is tolerable in combination with dexamethasone
  - No DLTs were seen across the 4 dose levels tested
  - No TEAE leading to treatment discontinuation and No TEAE leading to death.
  - Toxicities were rare and manageable. The only hematologic toxicity seen was 1 case of grade 2 neutropenia, which did not lead to dose modifications or discontinuation
- BGB-11417 demonstrated activity at all tested dose levels, and most patients achieved disease control
  - One patient achieved CR in the 160 mg cohort
- Dose escalation is ongoing and RP2D was not achieved

Data cutoff: 16 September 2022.
aThe 95% CI was estimated using the Clopper-Pearson method
BRR=better response rate, CI=confidence interval, CR=complete response, MR=minor response, ORR=overall response rate, PD=progressive disease, PR=partial response, sCR=stringent complete response, SD=stable disease, VGPR=very good partial response
Quach H et al. Poster presented at ASH 2022 Abstract 3235



BeiGene

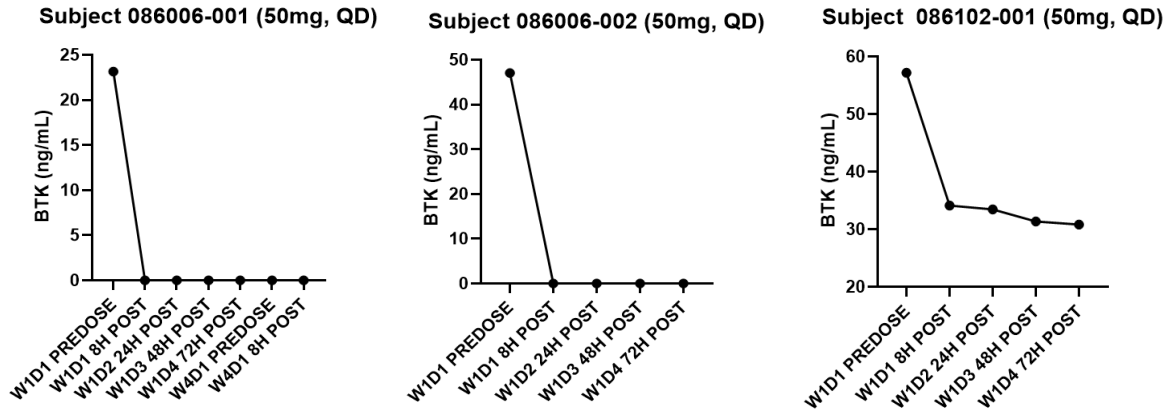
BGB-16673 (BTK-CDAC)

Mehrdad Mobasher, M.D., M.P.H.
Chief Medical Officer, Hematology

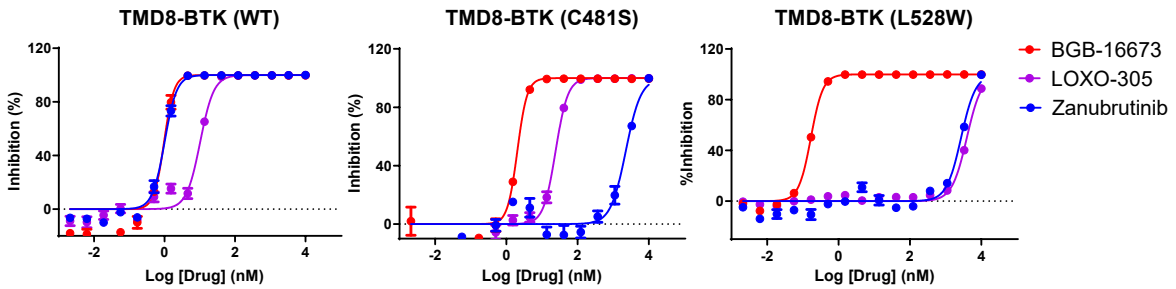
BTK Chimeric Degradation Activating Compound for B-Cell Malignancies Showing Promise in Clinic

- Targeting BTK via an alternative mechanism
- **New generation** BTK inhibitor to enhance BTK expertise
  - To overcome BTK kinase inhibitor resistance
  - To destroy non-kinase (scaffolding) function
- **BGB-16673**, BeiGene's first CDAC molecule advanced to clinic
  - **2.5 years from program initiation to clinic**
  - Good pharmacological properties
    - No IMiD activity
    - Highly potent and selective
    - Good oral bioavailability and long $t_{1/2}$
  - **Complete BTK degradation and clinical response observed at the first dose level**, 50 mg

Deep, Rapid & Sustainable BTK Degradation Observed at the First Dose Level in Phase 1 Study (50 mg)



BGB-16673 can Overcome both Zanubrutinib and LOXO-305 Resistance



IMiD: immunomodulatory imide drug

Key Opportunities Within B-cell Malignancies and Expansion to Other Hematological Malignancies

		BTKi	BCL2i	BTK CDAC	IO/IO combo
B-cell Malignancies	CLL/SLL				
	MCL				
	MZL				
	FL				
	WM				
	DLBCL				
cHL					
AML	AML				
MDS	MDS				
Multiple Myeloma	MM				

- Monotherapy
- Mono/Combo with internal asset
- Mono/Combo with external asset
- Combo with external asset
- Combo with internal and external asset
- Mono/combo with internal and external asset

Key Takeaways

John V. Oyler

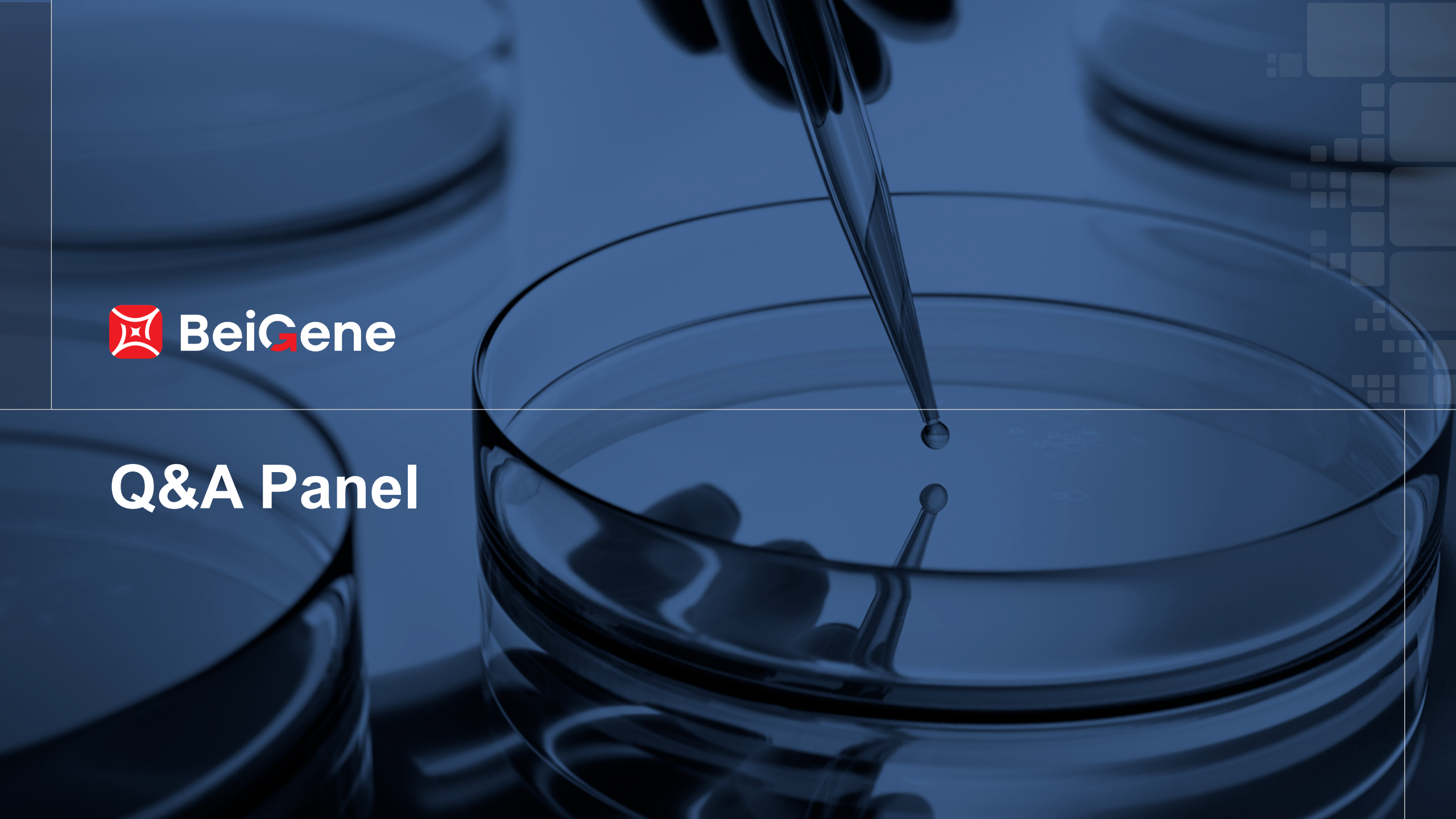
Co-Founder, Chairman, and CEO

Key Takeaways

- Exciting and growing hematology pipeline
  - BRUKINSA (BTKi): *Designed to be best-in-class BTK inhibitor*
    - Only BTKi demonstrating PFS superiority vs. IMBRUVICA® in a head-to-head study
    - Broad clinical development program with approvals in 60+ markets and four indications
  - BGB-11417 (BCL-2i): *Potentially transformational asset*
    - Early clinical PK/PD data support the hypothesis that BGB-11417 has best-in-class potential
    - Potential registrational studies ongoing and Phase 3 trials planned in large indications including CLL
  - BGB-16673 (BTK-CDAC): *Complete BTK degradation and clinical response observed at the first dose level*

- Committed to developing impactful medicines and making them more affordable and accessible

- Building unique competitive strategic advantages in research, clinical development, manufacturing and commercial



BeiGene

Q&A Panel

Q&A Participants

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Dr. Mark Lanasa
Chief Medical Officer, Solid Tumors

Julia Wang
Chief Financial Officer

Josh Neiman
Chief Commercial Officer, North America and Europe

Dr. Christiane Langer
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BeiGene
THANK YOU