

CaDAnCe-104, an Ongoing, Open-Label, Phase 1b/2 Master Protocol Study of Bruton Tyrosine Kinase Degradar BGB-16673 in Combination With Other Agents in Patients With Relapsed/Refractory B-Cell Malignancies

Chan Y. Cheah,^{1,3} Mohamed Shanavas,^{4,5} Julio C. Chavez,⁶ Hongyan Tong,⁷ Xiaoyun (Nicole) Li,⁸ Prasanna Kumar,⁸ Amit Agarwal,⁸ Mary Ann Anderson,^{9,10} Nitin Jain¹¹

¹Sir Charles Gairdner Hospital, Nedlands, WA, Australia; ²Medical School, University of Western Australia, Crawley, WA, Australia; ³Linear Clinical Research, Nedlands, WA, Australia; ⁴Mater Hospital, Brisbane, QLD, Australia; ⁵School of Medicine, University of Queensland, Herston, QLD, Australia; ⁶Mayo Clinic, Jacksonville, FL, USA; ⁷The First Affiliated Hospital, School of Medicine, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China; ⁸BeOne Medicines, Ltd, San Carlos, CA, USA; ⁹Royal Melbourne Hospital and Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; ¹⁰The Walter and Eliza Hall Institute, Melbourne, VIC, Australia; ¹¹The University of Texas MD Anderson Cancer Center, Houston, TX, USA

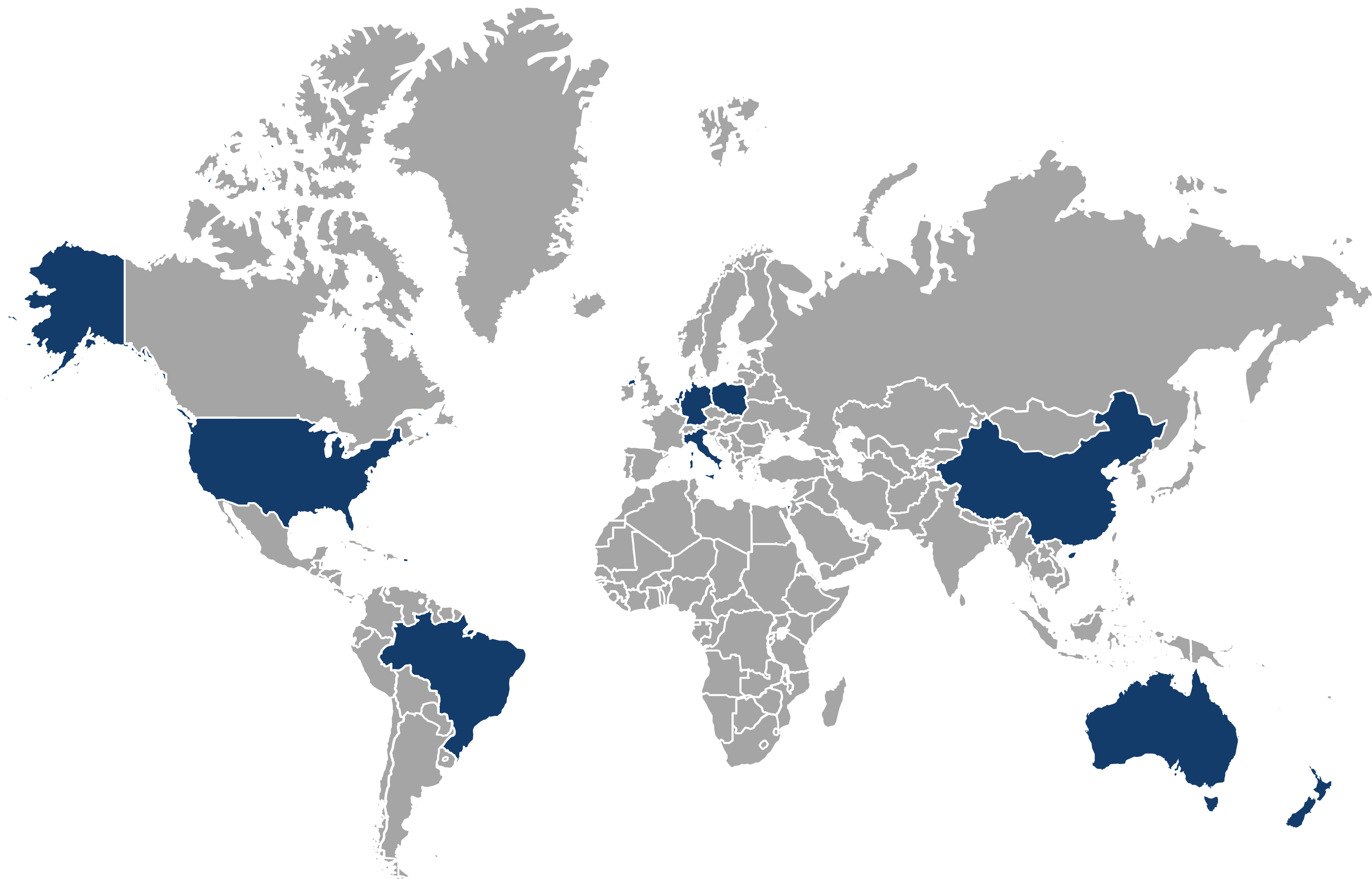
INTRODUCTION

- Bruton tyrosine kinase (BTK) inhibitors are effective treatment strategies for patients with certain B-cell malignancies, but most patients eventually experience disease progression, underscoring the need for novel therapeutic approaches including agents that can be used in combination with BTK inhibitors^{1,4}
- BGB-16673 is an orally available protein degrader that blocks BTK signaling by tagging BTK for degradation through the cell’s proteasome pathway, leading to tumor regression⁵
- By degrading BTK, BGB-16673 disrupts both inherent BTK catalytic activity and its separate protein scaffolding functions, in contrast to small molecule BTK inhibitors that temporarily block BTK catalytic activity alone^{6,7}
- The elimination of BTK by degradation may be effective against treatment-resistant BTK mutants that have been shown to limit the efficacy of current BTK inhibitors⁶
- In preclinical models, BGB-16673 degraded both wild-type BTK and mutant forms of BTK that have shown resistance to covalent and noncovalent BTK inhibitors; additionally, BGB-16673 showed central nervous system penetration^{5,8}
- In a clinical study, BGB-16673 led to substantial reductions in BTK protein levels in peripheral blood and tumor tissue⁹
- In the CaDAnCe-101 study (BGB-16673-101; NCT05006716), BGB-16673 monotherapy was well tolerated and demonstrated antitumor activity in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), Waldenström macroglobulinemia (WM), follicular lymphoma (FL), and marginal zone lymphoma (MZL)¹⁰⁻¹²
- This presentation outlines the study design of CaDAnCe-104 (BGB-16673-104; NCT06634589), an ongoing phase 1b/2 trial to evaluate the safety and efficacy of BGB-16673 in combination with other agents in patients with selected relapsed/refractory B-cell malignancies

STUDY STATUS

- Enrollment for CaDAnCe-104 phase 1 began in November 2024, and the trial is currently recruiting
- This study has 50 locations across the US, Australia, Brazil, China, Germany, Italy, New Zealand, and Poland (**Figure 1**), with an estimated enrollment of 330 patients in phase 1

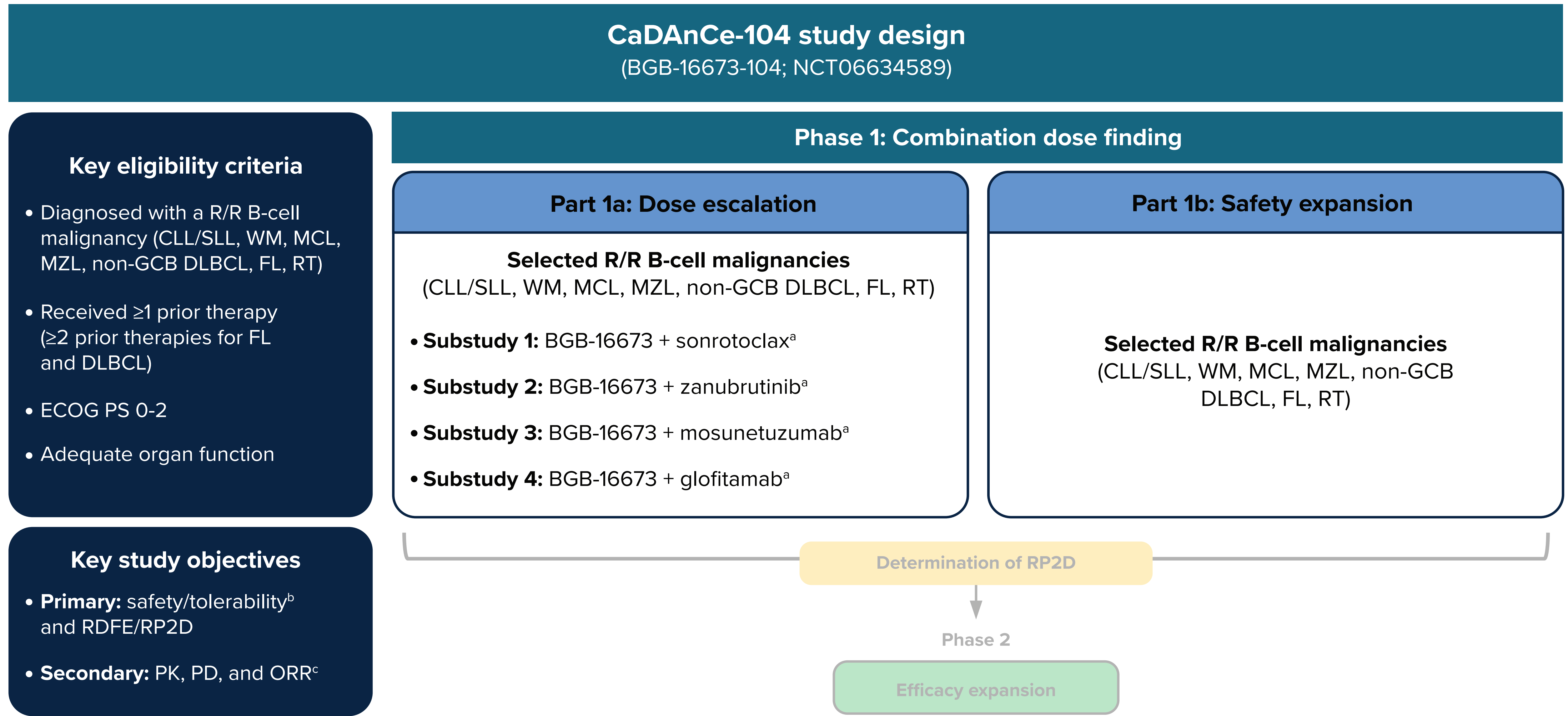
Figure 1. CaDAnCe-104 Study Sites (Planned)



METHODS

- CaDAnCe-104 (BGB-16673-104; NCT06634589) is a phase 1b/2, open-label, master protocol study comprising four substudies investigating the safety and effectiveness of BGB-16673 in combination with sonrotoclax, zanubrutinib, mosunetuzumab, or glofitamab in patients with selected relapsed/refractory B-cell malignancies, including CLL/SLL, WM, mantle cell lymphoma (MCL), MZL, non–germinal center B–cell like diffuse large B-cell lymphoma (non-GCB DLBCL), FL, and Richter transformation (RT) (**Figure 2**)
 - The primary objectives are to evaluate safety and tolerability per NCI-CTCAE v5.0 and to identify the recommended dose for expansion (RDFE) in part 1a and the recommended phase 2 dose in part 1b
 - The secondary objectives are to assess overall response rate, duration of response, and time to response at each dose level in part 1a and at the selected RDFE(s) and to assess the pharmacokinetics of BGB-16673 and combination drugs in their respective substudies
 - In addition, exploratory analyses will be conducted using patient samples to assess predictive, prognostic, and pharmacodynamic biomarkers

Figure 2. CaDAnCe-104 Study Design



^aTreatment will be administered until progressive disease, unacceptable toxicity, withdrawal of consent, or other criteria are met for treatment discontinuation. ^bSafety will be assessed according to NCI-CTCAE v5.0 in all patients. ^cResponse will be assessed per Lugano criteria for SLL, DLBCL, FL, RT, MZL, and MCL; iwCLL 2018 criteria for CLL; and IWWM-11 criteria for WM.
Abbreviations: CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; GCB, germinal center B-cell; iwCLL, International Workshop on Chronic Lymphocytic Leukemia; IWWM, Internal Workshop on Waldenström Macroglobulinemia; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; ORR, overall response rate; PD, pharmacodynamics; PK, pharmacokinetics; R/R, relapsed/refractory; RDFE, recommended dose for expansion; RP2D, recommended phase 2 dose; RT, Richter transformation; WM, Waldenström macroglobulinemia.

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