

Trial in progress: A first-in-human phase 1a/b study of BGB-58067, an MTA-cooperative PRMT5 inhibitor, in patients with advanced solid tumors and MTAP deficiency

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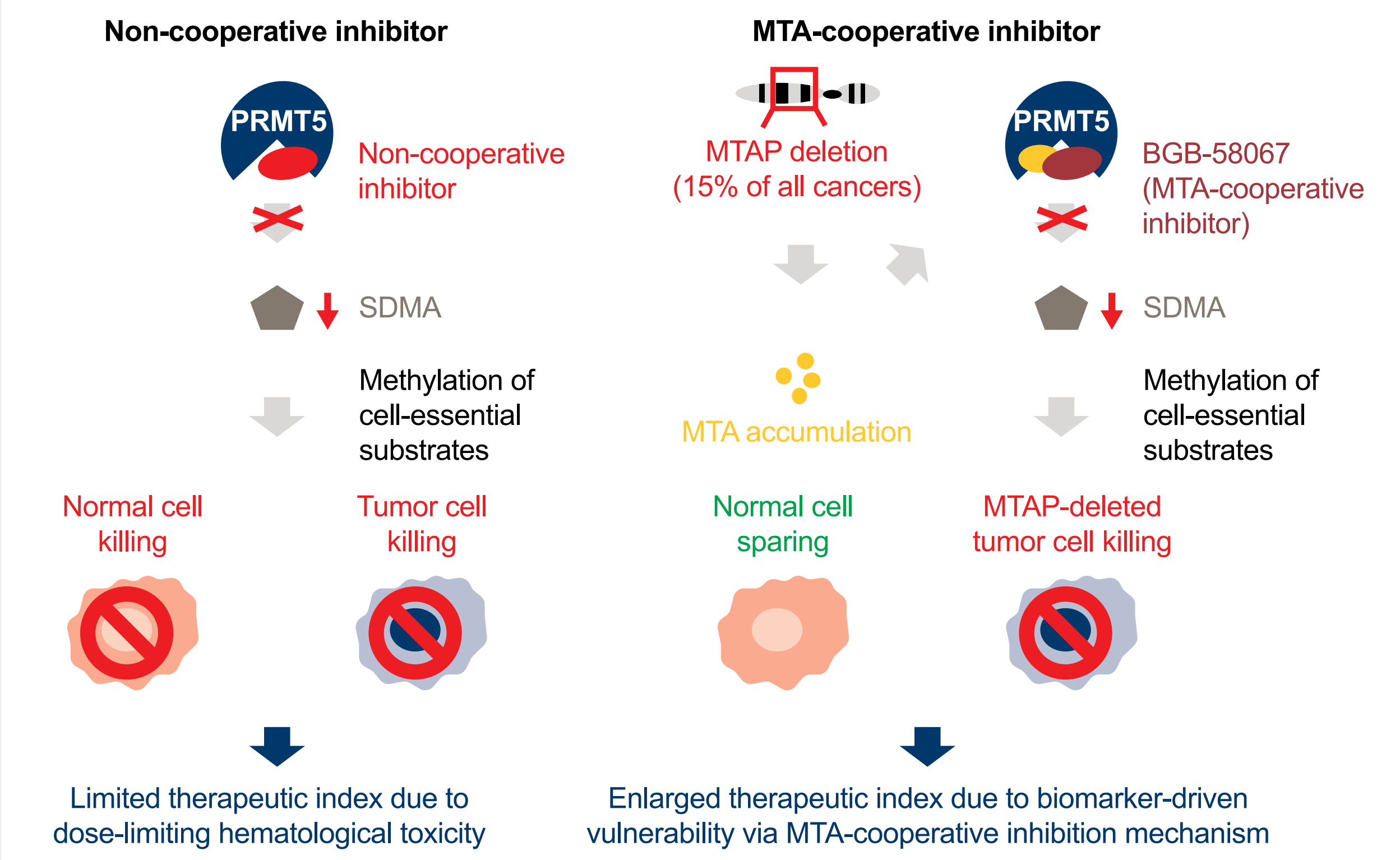
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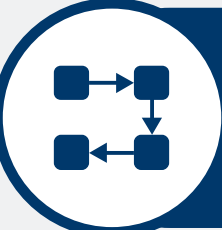
Introduction

- Protein arginine methyltransferase 5 (PRMT5) is a type II arginine methyltransferase that catalyzes the formation of monomethylated arginine (MMA) and symmetric dimethylarginine
 - PRMT5 participates in the methylation of substrates involved in cellular activities, including transcription, RNA splicing, DNA damage repair, apoptosis, and cell-cycle regulation¹
 - PRMT5 may act as an oncogene,¹ with its overexpression associated with poor outcomes in a range of cancers, including lung, colon, pancreas, and bladder cancer, and glioblastoma multiforme¹⁻⁵
- Homozygous loss of the *methylthioadenosine phosphorylase* (MTAP) gene occurs in 15% of all tumor types,⁶ leading to the accumulation of methylthioadenosine (MTA), which partially inhibits PRMT5 and increases the susceptibility of these tumor cells to additional PRMT5 inhibition⁷⁻⁹

Figure 1. Mechanism of Action of BGB-58067



- BGB-58067 is an oral, highly potent, brain-penetrant, MTA-cooperative PRMT5 inhibitor that selectively inhibits PRMT5 in tumors with MTAP deletion (**Figure 1**)
 - Preclinical evidence has shown the effectiveness of BGB-58067 in inhibiting PRMT5-mediated signaling and in its *in vivo* antitumor activity¹⁰
- BGB-58067 is being assessed as monotherapy in a first-in-human, phase 1a/b, open-label, international, multicenter trial in patients with advanced solid tumors with MTAP deficiency (NCT06589596)



Methods

Trial design

- This first-in-human, phase 1, open-label, international, multicenter trial consists of two parts: phase 1a (dose escalation/safety expansion) and phase 1b (dose expansion/optimization) (**Figure 2**)

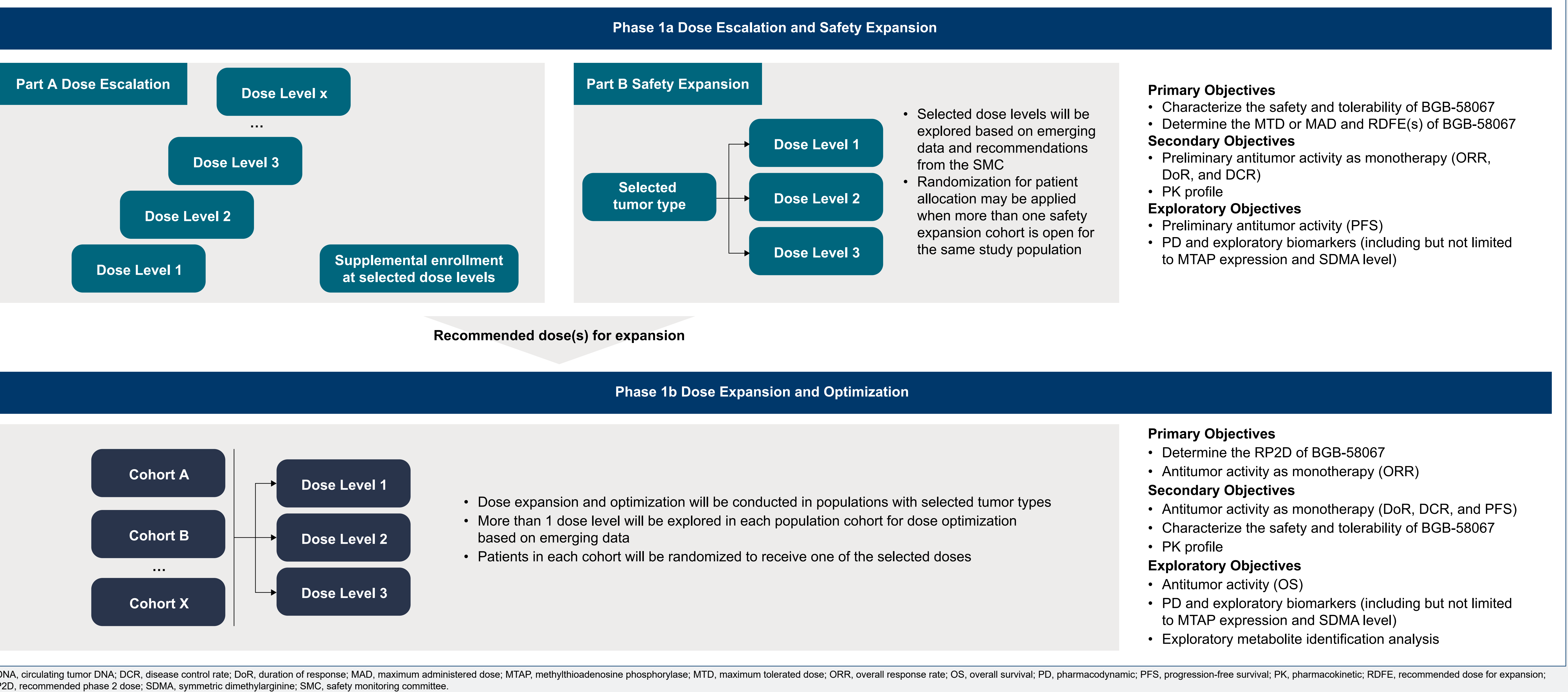
Key eligibility criteria

- Inclusion Criteria:
 - Patients with advanced, metastatic, or unresectable solid tumors, who have previously received standard systemic therapy or for whom treatment is not available or not tolerated
 - ECOG Performance Status of 0 or 1 or Karnofsky Performance Scale ≥ 70
 - Life expectancy ≥ 3 months
 - Evidence of homozygous loss of *MTAP* or lost MTAP expression in the tumor tissue
- Exclusion Criteria:
 - Prior treatment with any PRMT5 inhibitor or methionine adenosyltransferase 2a inhibitor
 - Active leptomeningeal disease or symptomatic spinal cord compression
 - Uncontrollable pleural effusion, pericardial effusion, or ascites requiring frequent drainage
 - Any malignancy ≤ 2 years before first dose of study drug except for the specific cancer under investigation in this study and any locally recurring cancer that has been treated curatively
- Please refer to ClinicalTrials.gov, NCT06589596, for further eligibility criteria

Analysis and Statistical Methods

- Dose escalation will be guided using the modified toxicity probability interval method¹¹
- Patient demographics, safety, pharmacokinetics, and efficacy will be summarized by dose level and for all patients. Quantitative data will be described by standard descriptive statistics. Qualitative data will be summarized by frequency tables with number and proportion in each category
- Efficacy endpoints such as overall response rate and disease control rate will be summarized by dose level along with their 95% confidence intervals. The time-to-event endpoints, including duration of response, progression-free survival and overall survival will be analyzed using the Kaplan–Meier method

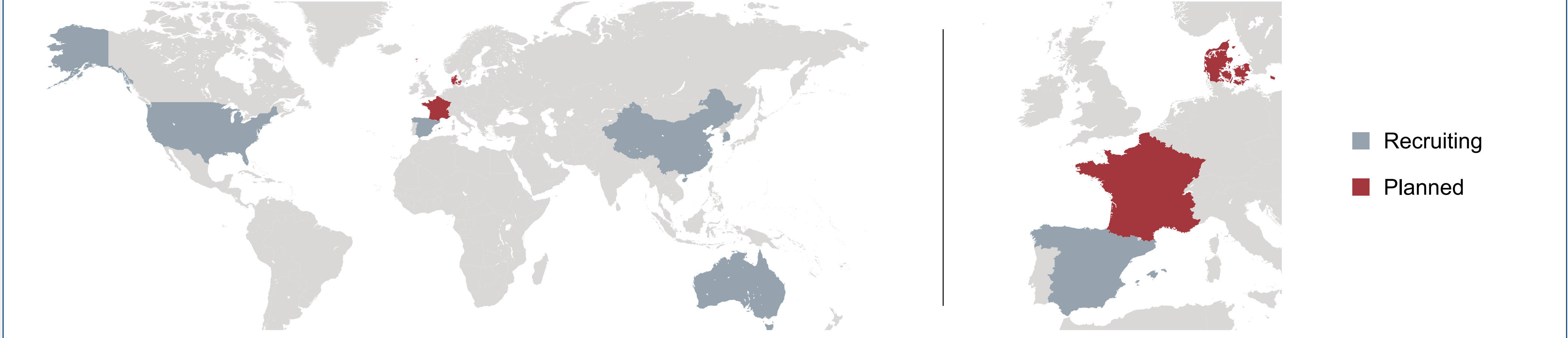
Figure 2. Study Design



Study Status

- This trial opened for enrolment in October 2024 and is anticipated to close in November 2026
- As of March 2025, this trial is actively recruiting patients in Australia, China, Korea, Spain, and the United States. For a list of participating sites, please refer to ClinicalTrials.gov, NCT06589596

Figure 3. Participating Countries



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Disclosures

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Tai Qin, Hayden Huang, Chunyu Wang, and Yan Dong are employees of BeiGene and may own company stock/stock options.

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