

# Trial in progress: A first-in-human phase 1a/b, dose-escalation/expansion study of BG-68501/ETX-197 (CDK2 inhibitor) as monotherapy or in combination with fulvestrant for patients with HR+/HER2- breast cancer and other advanced solid tumors

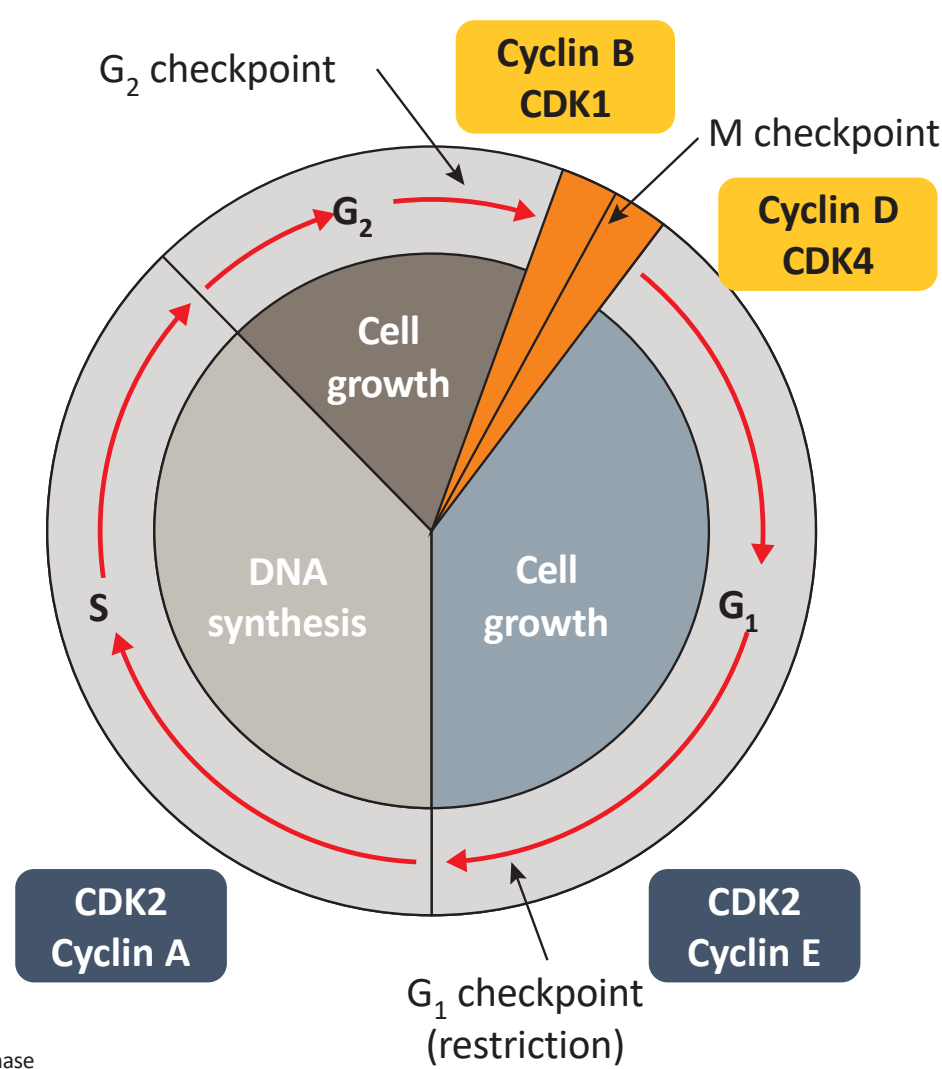
Minal Barve,<sup>1</sup> Jennifer Man,<sup>2</sup> Bruno Fang,<sup>3</sup> Alexander Philipovskiy,<sup>4</sup> Brian A. Van Tine,<sup>5</sup> Rohit Joshi,<sup>6</sup> Marion Carrigan,<sup>7</sup> Alejandra Ragone,<sup>7</sup> Hao Zheng,<sup>7</sup> Yang Liu,<sup>8</sup> Sally Baron Hay<sup>9</sup>  
<sup>1</sup>Mary Crowley Cancer Research, Dallas, TX, USA; <sup>2</sup>Blacktown Cancer and Haematology Centre, Blacktown, NSW, Australia; <sup>3</sup>Astera Cancer Care, East Brunswick, NJ, USA; <sup>4</sup>Florida Cancer Specialists and Research Institute/Sarah Cannon Research Institute, Lake Mary, FL, USA; <sup>5</sup>Washington University School of Medicine, Saint Louis, MO, USA; <sup>6</sup>Cancer Research SA, Adelaide, SA, Australia; <sup>7</sup>BeiGene USA, Inc, San Mateo, CA, USA; <sup>8</sup>BeiGene (Shanghai) Co., Ltd, Shanghai, China; <sup>9</sup>University of Sydney, Sydney, NSW, Australia

Poster No: P4-08-20  
 San Antonio Breast Cancer Symposium  
 December 10-13, 2024

## Introduction

- CDKs are important regulators of cell cycle progression (Figure 1)
- Inhibition of CDKs has been shown to have antiproliferative effects on tumor cells<sup>1</sup>
- Targeting both CDK2 and CDK4/6 may lead to improved antitumor activity<sup>2,3</sup>
- BG-68501/ETX-197 is a potent inhibitor of CDK2 with preclinical evidence showing strong antitumor activity and superior selectivity for CDK2 over other CDK family members<sup>4</sup>
- This is a first-in-human, phase 1a/b, open-label, multicenter trial to evaluate the safety, tolerability, PK, and preliminary antitumor activity of oral BG-68501/ETX-197
- BG-68501/ETX-197 will be given as monotherapy for patients with advanced, nonresectable, or metastatic solid tumors, and in combination with fulvestrant ± BGB-43395 (a highly potent, selective, and orally available CDK4 inhibitor<sup>3</sup>) for patients with HR+/HER2- breast cancer (BC) (NCT06257264)

**Figure 1. CDK2 Forms a Complex with Cyclin E and Cyclin A to Regulate the G<sub>1</sub>/S and S/G<sub>2</sub> Cell Cycle Transitions**



## Methods

### Study design

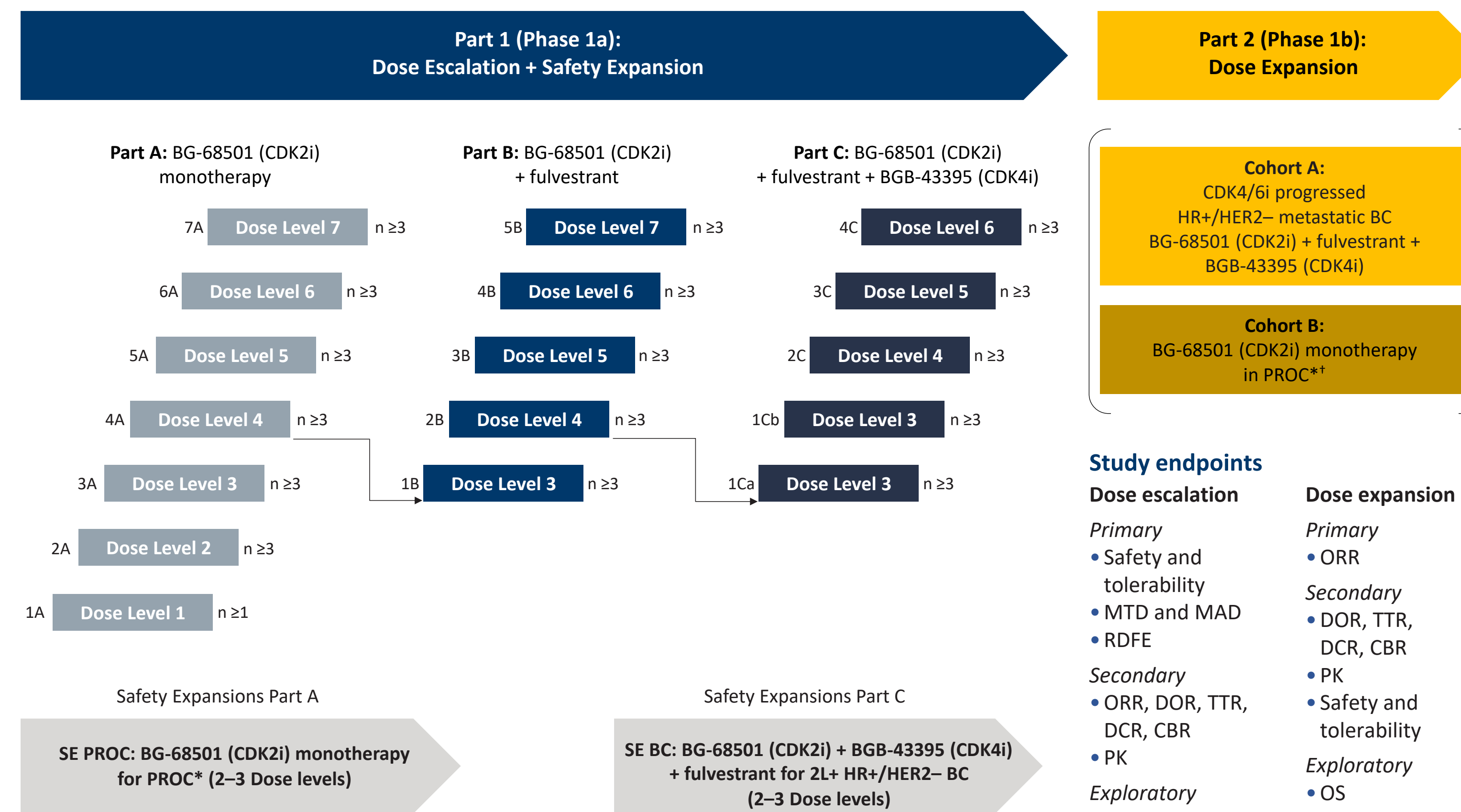
- This is a phase 1, open-label, multicenter trial consisting of two parts: dose escalation and expansion (Figure 2)

### Figure 2. Study Design

#### Key eligibility criteria

- ≥18 years
- Advanced or metastatic solid tumors potentially associated with CDK2 dependency
- Prior available SOC systemic therapies
  - For HR+/HER2- BC: ≥1L for advanced or metastatic disease, including prior ET and a CDK4/6i (where approved/available) in either the adjuvant or advanced/metastatic setting
  - For PROC: ≥1L of platinum-containing CT for advanced disease; ≤4L in the advanced/metastatic setting
- GnRH agonists for ovarian function suppression (unless menopausal)
- GnRH agonists for males treated with fulvestrant
- ECOG PS ≤1
- Measurable disease per RECIST v1.1
- No uncontrolled/untreated brain metastases
- No prior therapy selectively targeting CDK2

Inclusion criteria for the Safety Expansion Parts A and C matches inclusion criteria for the equivalent Phase 1b dose expansion cohorts.  
 \*Including fallopian tube or primary peritoneal cancer. †Patients may be selected based on cyclin E1 expression; cut-off to be determined.  
 2L+, second-line or greater; CBR, clinical benefit rate; DCR, disease control rate; DOR, duration of response; ET, endocrine therapy; MAD, maximum administered dose; MTD, maximum tolerated dose; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; PROC, platinum-refractory or resistant serous ovarian cancer; RDFE, recommended dose for expansion; RECIST, response evaluation criteria in solid tumors; SE, safety expansion; TTR, time to response.



### Study endpoints

- |                           |                           |
|---------------------------|---------------------------|
| <b>Dose escalation</b>    | <b>Dose expansion</b>     |
| <i>Primary</i>            | <i>Primary</i>            |
| • Safety and tolerability | • ORR                     |
| • MTD and MAD             | <i>Secondary</i>          |
| • RDFE                    | • DOR, TTR, DCR, CBR      |
| <i>Secondary</i>          | • PK                      |
| • ORR, DOR, TTR, DCR, CBR | • Safety and tolerability |
| • PK                      | <i>Exploratory</i>        |
| <i>Exploratory</i>        | • OS                      |
| • PFS                     | • Biomarkers              |
| • Biomarkers              |                           |

## Methods

### Statistical methods

- The dose escalation will proceed according to the modified toxicity probability interval-2 method<sup>5,6</sup>
- Data collected will be reported using summary tables and figures. Categorical variables will be summarized by frequency distributions, and continuous variables will be summarized by descriptive statistics
- For time-to-event variables, percentages of patients experiencing that event will be presented, and median time-to-event will be estimated using Kaplan-Meier methodology

## Conclusions

- BG-68501/ETX-197 is being assessed as monotherapy for patients with advanced solid tumors and in combination with fulvestrant ± BGB-43395 for patients with HR+/HER2- BC in a first-in-human, phase 1, dose-escalation and expansion study
- This study will provide insights into the clinical effects of targeting CDK2 in solid tumors
- As of October 29, 2024, recruitment is ongoing, with 11 sites open across 3 countries (Australia, China, and US) and 21 patients dosed

## Contact

Dr Minal Barve  
 Mary Crowley Cancer Research, Dallas, TX, USA  
 MBarve@MaryCrowley.org

## References

1. Li J, et al. *JAMA Netw Open* 2020;3:e2020312.
2. Kudo R, et al. *Cancer Cell* 2024;42:1-17.
3. Yap TA, et al. Presented at the San Antonio Breast Cancer Symposium, TX, USA, December 10–13, 2024.
4. Banerjee D, et al. Presented at the San Antonio Breast Cancer Symposium, TX, USA, December 10–13, 2024.
5. Guo W, et al. *Contemp Clin Trials* 2017;58:23-33.
6. Ji Y, et al. *Clin Trials* 2007;4:235-44.

## Acknowledgments

We would like to thank the investigators, site support staff, and especially the patients for participating in this study. This study is sponsored by BeiGene. Medical writing support was provided by AMICULUM USA, with funding provided by BeiGene

Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from SABCS® and the author of this poster.

