A first-in-human, phase 1a/b, dose-escalation/expansion study of BG-68501, a selective CDK2 inhibitor, as monotherapy or in combination with fulvestrant for patients with HR+/HER2- breast cancer and other advanced solid tumors: First disclosure of clinical data

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Background: CDK2 inhibition could represent a novel treatment (tx) option for patients (pts) with resistance to CDK4/6 inhibitors (CDK4/6i) and/or increased cyclin E1 activity. BG-68501 is a highly potent CDK2 inhibitor with high CDK2 selectivity (~100x) vs other CDK family members. We present dose-escalation data of BG-68501 as monotherapy or in combination with fulvestrant in pts with HR+/HER2- metastatic breast cancer (BC) and advanced solid tumors (NCT06257264).

Methods: This is the dose-escalation phase of a first-in-human, phase 1a/b, open-label, multicenter study to evaluate the safety/tolerability, pharmacokinetic (PK), and pharmacodynamic (PD) profiles, and preliminary antitumor activity of BG-68501 in pts with advanced, nonresectable, or metastatic solid tumors, including HR+/HER2− BC. During dose escalation, sequential cohorts received increasing doses of BG-68501 as monotherapy or in combination with fulvestrant. Eligible pts are ≥18 yrs, with histologically or cytologically confirmed advanced or metastatic solid tumors associated with CDK2 dependency who have received ≥1 line of tx for advanced or metastatic disease and prior endocrine therapy and a CDK4/6i in either the adjuvant or advanced or metastatic setting for HR+/HER2− BC, or prior standard of care for all other advanced solid tumors.

Results: As of Jan 22, 2025, 41 pts (median age 63 yrs) have been enrolled. Eleven pts had BC (all received prior CDK4/6i), 12 had ovarian cancer (OC), 7 had endometrial cancer, and the remaining 11 pts had other tumor types. To date, 6 dose levels (DLs) of BG-68501 monotherapy and 1 DL in combination with fulvestrant have been assessed. The median duration of exposure is 1.5 months. Treatment-emergent adverse events occurred in 39 pts (95.1%; grade ≥3, 26.8%), with the most common being nausea (56.1%; grade ≥3, 0%), vomiting (48.8%; grade ≥3, 0%), and fatigue (24.4%; grade ≥3, 0%); no DLTs have been observed. BG-68501 demonstrated a linear PK profile with clinical characteristics consistent with preclinical predictions; signs of TK1 reductions have been observed across DLs tested, including in heavily pretreated pts. Of the 24 efficacy-evaluable pts, 1 extensively pretreated HR+/HER2− BC pt experienced PR and 10 pts showed SD. Dose escalation is ongoing for both monotherapy as well as in combination with fulvestrant.

Conclusions: BG-68501 demonstrates a favorable safety/tolerability profile, with no DLTs observed to date during dose escalation. Extensively pretreated patients achieving PR and SD with monotherapy, coupled with signs of PD responses and a favorable safety profile, support continued assessment of BG-68501; updated clinical data will be presented at the time of the conference.