

## **First-in-human trial of BGB-58067, an MTA-Cooperative PRMT5 Inhibitor, in MTAP-deficient advanced tumors**

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**Background:** BGB-58067 is a potent, brain-penetrant, oral methylthioadenosine (MTA)-cooperative protein arginine methyltransferase 5 (PRMT5) inhibitor. It selectively binds to and stabilizes the catalytically inactive PRMT5/MTA complex and demonstrates antitumor activity in MTA phosphorylase (MTAP)-deleted tumor models. Initial phase 1a data from the first-in-human study of BGB-58067 (NCT06589596) are reported.

**Methods:** Patients (pts) with MTAP-deficient advanced tumors were enrolled to receive ascending doses (50-800 mg) of BGB-58067 QD. MTAP deficiency was assessed by local and/or central IHC or NGS tests. Endpoints included safety, antitumor activity, and PK and pharmacodynamic profiles. Antitumor activity was reported in all evaluable pts and in a subgroup with NSCLC receiving BGB-58067  $\geq 3$  months before data cutoff (DCO).

**Results:** At DCO (March 20, 2026), 163 pts with a median of 2 prior lines of therapy were enrolled. The largest cohort was NSCLC (N=80); 40% and 20% of pts had brain and liver metastases at baseline, respectively. There was an approximately linear and proportional increase in steady-state exposure of BGB-58067 from 50-800 mg. Target engagement was confirmed by symmetric dimethylarginine reduction in tumor tissue and blood. TRAEs occurred in 145 pts (89%); 58 (36%) were grade  $\geq 3$ . Most common TRAEs were nausea (34%), anemia (28%), fatigue (23%), and appetite decrease (23%). Five pts (3%) discontinued due to TRAEs. One dose-limiting toxicity (grade 4 platelet count decreased) was reported at 800 mg.

With a short median treatment follow-up of 3.6 months, unconfirmed ORR across tumor types (excluding CNS) was 24.6% (31/126) and a DCR of 73.0% (92/126). In the 41 efficacy-evaluable pts with NSCLC at recommended phase 2 dose ranges, unconfirmed ORR was 31.7% and DCR was 68.3%; overall responses may deepen over longer follow-up. Responses were observed across histological subtypes and in pts with baseline brain metastases, with evidence of intracranial response.

**Conclusions:** BGB-58067 demonstrated encouraging antitumor activity in MTAP-deficient advanced tumors, including NSCLC, with a tolerable safety profile. These results support further evaluation of BGB-58067 in MTAP-deficient tumors.