A Phase 1/1b/2 Study Evaluating the Safety, Tolerability, PK, PD, and Efficacy of AMG 193 Alone and in Combination With Docetaxel in Subjects With Advanced MTAP-Null Solid Tumors

**Primary Endpoints:**
- Parts 1 and 2: Safety and Tolerability
- Part 3: ORR

**Key Secondary Endpoints:**
- Parts 1 and 2: PK
- Parts 1, 2, and 3: DCR, DoR, TTR, duration of SD, PFS, and OS
- Part 3 only: Safety

**Screening/enrollment**
- AMG 193 + Chemo (MTAP-null NSCLC)\(^c\)
- AMG 193 monotherapy (MTAP- or CDKN2A-null solid tumors)\(^a\)
- AMG 193 monotherapy (MTAP-null solid tumors) (Multiple-patient dose cohorts)\(^d\)
- AMG 193 + Chemo (MTAP-null NSCLC)\(^c\)
- AMG 193 + Chemo (MTAP-null NSCLC)\(^c\)
- AMG 193 (MTAP-null NSCLC)

**Parts**
- Part 1: Dose Exploration
  - AMG 193 monotherapy (MTAP- or CDKN2A-null solid tumors)\(^a\)
  - AMG 193 + Chemo (MTAP-null NSCLC)\(^c\)
- Part 1: Dose Expansion
  - AMG 193 monotherapy (MTAP-null solid tumors) (Multiple-patient dose cohorts)\(^d\)
- Part 2: Dose Exploration
  - AMG 193 + Chemo (MTAP-null NSCLC)\(^c\)
- Part 2: Dose Expansion
  - Combination MTD/RP2D
- Part 3: Evaluate ORR
  - AMG 193 (MTAP-null NSCLC)

\(^a\)Parts 1a and 1b: MTAP- or CDKN2A-null solid tumors; \(^b\)Part 1c: MTAP-null squamous NSCLC; Part 1d: MTAP-null adenocarcinoma NSCLC; Part 1e: MTAP-null BTC; Part 1f: MTAP-null HNSCC; Part 1g: MTAP-null pancreatic adenocarcinoma; Part 1h: MTAP-null solid tumors other than squamous or adenocarcinoma NSCLC, BTC, HNSCC, pancreatic adenocarcinoma, primary brain tumor, and lymphoma; \(^c\)Parts 2a and 2b: MTAP null NSCLC.
**Key Summary Point:**
This is an open-label, phase 1/1b/2 study evaluating the safety, tolerability, PK, PD, and efficacy of AMG 193 alone and in combination with chemotherapy in adult subjects with advanced MTAP-null solid tumors.

**Key Inclusion Criteria:**
- Adults (≥ 18 years old) with histologically confirmed metastatic or locally advanced solid tumors not amenable to curative treatment with surgery and/or radiation.
- Evidence of homozygous loss of CDKN2A (null) [Parts 1a/b only] and/or MTAP (null) in the tumor tissue or blood [Parts 1a–1h, Parts 2a/b] or lost MTAP expression in the tumor tissue [Parts 1a–1h, Parts 2a/b].
- Measurable disease per RECIST v1.1 criteria.
- ECOG PS of ≤ 1.
- Adequate hematopoietic, renal, cardiac, and liver function.
- Life expectancy ≥ 3 months in the opinion of the investigator.
- A total of 25 slides of archived tumor tissue FFPE (sample collected within 5 years) or an archival block must be available.
- For Part 1f (MTAP-null or lost MTAP expression HNSCC): Must be willing to undergo tumor biopsy.
- For Parts 1a and 1b backfill: Must be willing to undergo tumor biopsy, before start of and while on treatment.

**Key Exclusion Criteria:**
- Spinal cord compression or untreated brain metastases or leptomeningeal disease.
- Evidence of current interstitial lung disease or active SARS-COV2 infection.
- History of other malignancy within the past 2 years.
- Active infection.
- History of solid organ transplant.
- Prior treatment with an MAT2A inhibitor or a PRMT5 inhibitor or docetaxel [Part 2 only].
- Unresolved toxicity from prior anticancer therapy.
- Diagnosis of congenital short QT syndrome.
- Known positive test for HIV.
- Major surgery.
- Prior irradiation to 25% of the bone marrow.
- Live vaccine therapy within 4 weeks before study drug administration.
- Positive hepatitis B surface antigen or positive HCV RNA by PCR.

**Additional Information:**
- www.clinicaltrials.gov Identifier—NCT05094336