GAT017 Inclusion Criteria

Key Inclusion Criteria:

1. Has a histologically- or cytologically-confirmed diagnosis of advanced, unresectable or metastatic gastric adenocarcinoma, gastroesophageal junction adenocarcinoma, or esophageal adenocarcinoma.

2. Has measurable disease per RECIST 1.1 as assessed by the local site investigator/radiology.

3. Has received, and progressed on, at least 2 prior chemotherapy and/or immunotherapy regimens.

   Note: For the purpose of this study, perioperative, neoadjuvant, and adjuvant chemotherapy regimens will NOT count as a prior regimen, unless the patient progressed while receiving adjuvant therapy or within 6 months of receiving adjuvant treatment.

   Note: Previous treatment regimens must have included a fluoropyrimidine and platinum doublet (as part of either a line of therapy or adjuvant treatment).

   Note: Prior immunotherapy may have been received alone or in combination with fluoropyrimidine and platinum-based chemotherapy.

4. Participants are eligible regardless of HER2 status. If HER2 status is unknown, sites should follow local standards to determine if HER2 testing is required as SOC. Participants who are HER2+ must have previously received trastuzumab where available/appropriate.

   Note: Participants who received prior trastuzumab-deruxtecan/T-DXd (topoisomerase 1 inhibitor-based ADC) in any line are not eligible.

5. Has provided tumor tissue sample for determination of TROP2 status by the central laboratory before randomization for stratification.

6. AEs due to previous anticancer therapies must have recovered to Grade ≤ 1 or baseline (except for alopecia and vitiligo). Participants with endocrine related AEs who are adequately treated with hormone replacement therapy are eligible.

7. Participants who may receive trifluridine-tipiracil must have the ability to swallow oral medication.

8. ECOG 0-1 (within 3 days of randomization)