**SGNTUC-019 PHASE 2 BASKET STUDY OF TUCATINIB AND TRASTUZUMAB IN SOLID TUMORS WITH HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 ALTERATIONS: UTERINE AND CERVICAL CANCER COHORTS**

**Background**

- Tucatinib (TUC), a highly selective HER2-directed TKI without significant EGFR inhibition, approved in multiple regions in combination with trastuzumab and capecitabine for HER2+ metastatic breast cancer.
- In HER2+ and HER2-mutated xenograft models, dual targeting of HER2 with the combination of TUC and trastuzumab (Tras) showed superior activity compared to either agent alone.1,2
- The prognoses of advanced cervical and uterine cancers are poor, with 5-year overall survival rates for metastatic diseases of 10% and 9%, respectively.3,4
- HER2 overexpression and amplification occur in 21% and 0.5%–14% of cases for cervical cancer, and 18%–80% and 4%–59% of cases for uterine cancers, respectively.5,6
- The SGNTUC-019 basket study (NCT04579380) is evaluating TUC in combination with Tras in patients with HER2+ or HER2-mutated solid tumors, including cohorts of patients with HER2+ cervical or uterine cancers.

**Tucatinib Mechanism of Action**

**Study Design**

**Primary Objective**

To evaluate the antitumor activity of TUC combined with Tras

**Secondary Objective**

To evaluate the safety and tolerability of TUC combined with Tras and the interaction with HER2 status in patients with metastatic breast cancer.

**Study Population**

- In Stage 1, 12 response-evaluable patients will be enrolled in both Cohorts 1 and 2 with HER2+ cervical and uterine cancers.
- Stage 2 will be opened for both Cohorts 1 and 2 to enroll 30 response-evaluable patients total in each cohort if 22 responses are observed in either cohort in Stage 1
- According to the predicted probability of success (PPoS)7, having ≥2 responders in each cohort means it is likely the objective response rate (ORR) exceeds 15%.
- Patients with HER2-mutated cervical and uterine cancers will be enrolled in Cohort 9; specific cohorts may be opened if enrollment is sufficient.

**Eligibility**

**Key Inclusion Criteria**

- Histologically or cytologically confirmed, locally-advanced unresectable, or metastatic, HER2+ or HER2-mutated solid tumors;

**Key Exclusion Criteria**

- HER2+ breast cancer, CRC, or gastric or gastroesophageal junction adenocarcinoma
- Prior HER2 directed therapy; patients with uterine serous carcinoma or HER2-mutated gastric or gastroesophageal junction adenocarcinoma
- HER2 overexpression/amplification may have received prior Tras
- Mucinous carcinoma or unstable anemia within 6 months, or clinically significant cardiomyopathy disease
- Known active HBV, HCV, or HIV infection or chronic liver disease
- Active CNS lesions ≥2 cm until approved by medical monitor

**Assessments**

- Disease assessments per RECIST v1.1: q6 weeks for 24 weeks, then q12 weeks.
- Safety assessments: AE, SAE, AESI, treatment modifications, laboratory assessments (metabolic panel, CBC with differential, and eGFR), vital signs, LVEF every 12 weeks, and ECG at baseline and EOT.

**Summary**

- SGNTUC-019 is a basket study evaluating TUC in combination with Tras in previously treated patients with HER2 overexpressed/amplified or HER2-mutated solid tumors, including cohorts of patients with locally-advanced unresectable or metastatic cervical or uterine cancer.
- Approximately 75 sites are planned for the Europe, US, and Asia-Pacific region. The study is open and enrolling in all regions.