SNS-595: Preliminary Results Of Two Phase 2 Second Line Studies In Lung Cancer

SNS-595 is a novel cell-cycle inhibitor that induces DNA damage responses, G2 arrest, and apoptosis. SNS-595 currently is being tested clinically in AML and ovarian cancer.

**Objectives:** To assess the response rate (RR), using RECIST criteria, patient safety, and time to progression (TTP), duration of response (DOR), and overall survival (OS) in patients (pts) with refractory (Ref) and sensitive (Sen) SCLC and advanced NSCLC treated with SNS-595.

**Methods:** In both studies, SNS-595 was given q3 weekly at a dose of 48mg/m² for up to 8 cycles. Both studies used a 2×2 stage Fleming design. The SCLC study was stratified, refractory (Ref = relapsed <90 days after end of initial therapy or never responded) and sensitive (Sen = relapse >90 days after response to initial therapy). The SCLC study was powered to detect a 35% ORR for the Ref and a 50% ORR for the Sen strata. The study enrolled 20 pts in stage 1 for both strata and required at least 1 response in the Ref and 2 responses in the Sen for continuation to stage 2 and enrollment of 20 more pts in each stratum. The SCLC study was powered to detect a 15% ORR. The study required a minimum of 1 response in the first 2 pts for study continuation to study stage 2 with 20 more pts. The primary dose limiting toxicity (DLT) was neutropenia. The Incidence of febrile neutropenia was lowest for SCLC sensitive cohort. The incidence of Grade 3/4 neutropenia (15%) was much lower compared to previous studies.

**SAFETY DATA**
- **Primary DLT:** Neutropenia
- **Incidence of Grade 3/4 neutropenia:** 15%
- **Incidence of febrile neutropenia:** Lowest for SCLC sensitive cohort
- **Other adverse events:** Pneumonia, Diarrhea, Anemia

**RESULTS**
- **Phase 1:** Median survival 2.9 months, 12 week ORR 34%, and 1 year survival 10%
- **Phase 2:** RR 30%, DOR 12 weeks, OS 6 months

**CONCLUSIONS AND FUTURE DIRECTIONS**
- SNS-595 demonstrates single agent activity in 2nd line lung cancer (NSCLC and SCLC) patient populations.
- SNS-595 was most active in SCLC sensitive population with 2/22 (9%) ORR and 16/22 (72%) stable disease.
- The incidence of Grade 3/4 neutropenia was lower in the lung cancer patients in this study (15%) or less.
- Further evaluation of SNS-595 in 2nd line SCLC sensitive patients should be at 60mg/m², the likely starting dose for minimally pre-treated patients.
- The nonclinical combination studies previously which show additivity or synergy with commonly used agents, together with the evidence of clinical activity, suggest that further exploration of SNS-595 in combination with other chemotherapeutic agents is warranted.