Ex Vivo Activity of SNS-595 Against Biopsies of Acute Myeloid Leukemia, Triple Negative Breast and Ovarian Cancers Supports Ongoing and Potential Clinical Indications

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**Abstract**

SNS-595 is a replication-dependent agent that induces DNA damage, irreversible G2 arrest and apoptosis by DNA intercalation and poisoning of topoisomerase II. SNS-595 is under clinical investigation in acute myeloid leukemia and ovarian cancer. Clinical responses have been observed in three indications (AML, AML with minimal residual disease, and ovarian cancer). SNS-595 inhibited proliferation >90% in 13/20 samples (65%) and >80% in 17/20 samples (85%). Activity was observed in clinically relevant concentrations, and 24 doxorubicin-resistant samples were sensitive to SNS-595. Potent antiproliferative activity of SNS-595 has previously been reported against 17 primary ovarian biopsies (McCormick, EORTC-2017). These data were extended by 2 samples and supported with expression profiling of the potential sensitivity biomarkers. At clinically relevant concentrations, the activity of SNS-595 compared favorably with platinum, etoposide and doxorubicin; however patient samples that were resistant to these agents were sensitive to SNS-595. Expression levels of DNA-PKcs and active p53 were determined in ovarian samples to test the importance of DNA-PKcs in repairing SNS-595 induced DNA damage (West et al, 2006). Levels of p53 and p73 were also assessed by IHC, having been associated with sensitivity in triple negative breast cancers (Ewing et al, 2007). Surprisingly, p53 and p73 levels were very absent in breast and ovarian samples. SNS-595 retained potent activity in the presence of DNA-PKcs and regardless of the observed levels of p53 and p73.

**Summary & Conclusions**

- SNS-595 is active against ovarian tumor biopsies that are resistant to doxorubicin and/or etoposide.
- Establishment of SNS-595 Concentrations for Correlative Study in AML
- Objective responses have been observed in patients with relapsed/refractory AML and platinum-resistant ovarian cancer and who have failed anthracycline-based therapies including 7+3 and Doxil®.
- SNS-595 potently inhibits proliferation of breast and ovarian cancer biopsies at clinically relevant concentrations.
- SNS-595 is in phase 2 trials as a single agent in both platinum resistant ovarian cancer and elderly, untreated AML patients and is in a phase 1b clinical study in combination with cytarabine in relapsed/refractory AML.
- The data presented here support the ongoing clinical studies as well as the potential for investigation of SNS-595 in breast cancer.

**Additional SNS-595 posters 1859 and 1860**