Sanofi	SSR97225
Mechanism of Action	β-Tubulin-binding agent with dual mechanism
Overview	SSR97225 is a novel tubulin-binding antimitotic agent with a potential dual mechanism of action possessing both anti-mitotic and anti-vascular activities. β-tubulin-binding experiments indicate that the binding site of SSR97225 differs from that of known tubulin binding reference agents such as paclitaxel, colchicine and vincristine. SSR97225 demonstrated submicromolar *in vitro* inhibition of tumor cell proliferation, including multidrug resistant cell lines (MDR1+), with a distinct profile compared to other reference agents. SSR97225 antivascular activity was also demonstrated *in vitro*. SSR97225 demonstrated an *in vivo* antitumor efficacy at low doses (25-50 mg/kg) in both solid and hematological tumor models including multidrug resistant models insensitive to many of the standard chemotherapeutic agents. When combined with other chemotherapies, this potent antitumor activity works additively, or synergistically in animal models.
Safety/Tolerability	At the time of the termination of the Phase 1 study, a total of 6 patients (3 patients each in Arms A [1 each at 9, 18. 36 mg/m^2 and B [3 at 3 mg/m^2]) received the study treatment. Four out of the 6 treated patients experienced at least 1 treatment-emergent adverse event (TEAE) during the study. One patient in Arm A experienced arthralgia and cough. Three patients in Arm B experienced TEAEs such as abdominal pain, diarrhea, disease progression, fatigue, increases in ALT/AST, blood alkaline phosphatase, bilirubin, and gamma GT, hyponatremia, arthralgia, pulmonary embolism, skin irritation, and deep vein thrombosis in 1 patient each; and anorexia in 2 patients. Most of these TEAEs were of Grade 1 or 2 and unrelated to the study treatment. One patient in Arm B who experienced a serious TEAE (Grade 3 deep vein thrombosis and later upgraded to Grade 4 pulmonary embolism at Cycle 1). The event was considered a dose-limiting toxicity (DLT) at Cycle 1. The patient's underlying metastatic pancreatic carcinoma and leukocytosis at baseline were contributing factors to deep vein thrombosis and pulmonary embolism. There was no cardiovascular adverse event observed in the study.
Additional Information	The initial nanoparticle formulation was manufactured by a CMO. A follow-up nanoparticle formulation using a different technology was subsequently explored, with another CMO, but terminated when the project was stopped. A Phase I study was initiated but terminated early due to the non-compliant drug concentration of the investigational product and the decision to discontinue the program due to competitive landscape. The Phase I included two study arms: Arm A, 1-hour IV infusion on Day 1 every 3 weeks; and Arm B, 1-hour IV infusion on Days 1, 8, and 15 every 3 weeks.
Suitable for and Exclusions	
Clinical Trials	http://clinicaltrials.gov/ct2/results?term=SSR97225
Publications	None