A PHASE I/RANDOMIZED PHASE II STUDY OF MLN0128 (TAK-228) VS. PAZOPANIB IN PATIENTS WITH LOCALLY ADVANCED/UNRESECTABLE AND/OR METASTATIC SARCOMA

Pre-Registration Eligibility Criteria (see Section 3.2)

Central pathology review submission (See §3.2.1)

Eligibility Criteria (see Section 3.3)

Documentation of disease subtypes listed in Section 3.3.1 by central review

Locally advanced or metastatic disease

Measureable disease and/or nonmeasureable as defined in Section 11.0

Prior treatment: Progression on at least one prior systemic chemotherapy for advanced, unresectable or metastatic disease. See Section 3.3.4 for additional information and exclusions.

Not pregnant and not nursing.

Age ≥ 18 years

ECOG Performance Status ≤ 1

Patients may not have any history of the diseases, conditions or disorders described in Section 3.3.8.

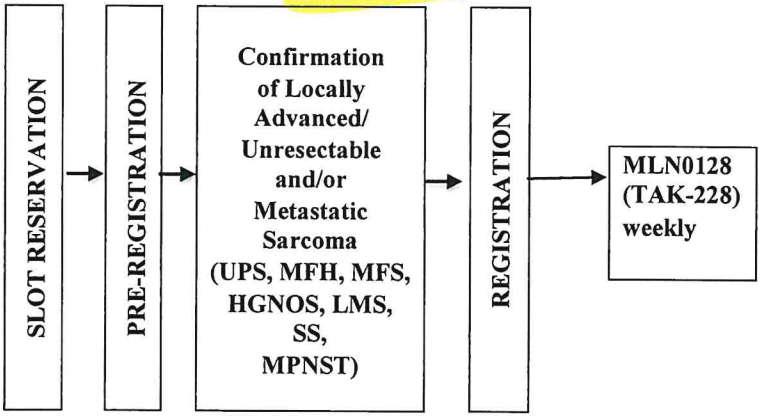
Concomitant medications: concomitant treatment with strong inhibitors of CYP3A4 inhibitors must discontinue the drug for 14 days prior to registration. Chronic concomitant treatment with strong CYP3A4 inducers is not allowed.

Required Initial Laboratory Values

Absolute neutrophil count (ANC)	≥ 1,500/mm^3
Platelet Count	≥ 100,000/mm^3
Creatinine	< 1.5 x ULN
Total Bilirubin	≤ 1.5 x ULN*
AST / ALT	≤ 3 x ULN*
UPC	≤ 1*
TSH	WNL

*See Section 3.3.9

Phase I Schema



The Phase I portion of this study will assess safety and tolerability of the new milled formulation of MLN0128 (TAK-228). The Phase I portion is a standard 3+3 design which includes dose level 0, 1, 2 for entry and dose modifications as per protocol. Patients may remain on treatment until disease progression, unacceptable toxicity, or withdrawal of consent.

Please Note: For the phase I portion of this study, patient enrollment will be facilitated using the Slot-Reservation System in conjunction with the Registration system on Oncology Patient Enrollment Network (OPEN). Prior to discussing protocol entry with the patient, all site staff must use the CTSU OPEN Slot Reservation System to insure that a slot on the protocol is available to the patient. Once a slot reservation confirmation is obtained, site staff may then proceed to pre-register the patient for central pathology review. Once eligibility has been confirmed centrally, then proceed to register patient onto the appropriate dose level.

Toxicity call attendance is required during the Phase I portion of the trial. See Section 7.1 for more information...