Supplemental Material

Inclusion Criteria - Patients must meet all the following criteria:
a. Be willing and able to provide written informed consent for the trial.
b. Must have a diagnosis of unresectable or metastatic soft tissue sarcoma that is histologically confirmed and not amenable to curative treatment with surgery or radiotherapy. Patients with Ewing's sarcoma, osteosarcoma, chondrosarcoma, Kaposi's sarcoma, gastrointestinal stromal tumors (GIST), clear cell sarcoma, alveolar soft part sarcoma and any other soft tissue or bone sarcoma felt to be chemotherapy resistant in the opinion of the Sponsor-Investigator will be excluded.
c. Must not have received prior treatment with an anthracycline chemotherapy (e.g., doxorubicin) and/or anti-PD-1/PD-L1 therapy.
d. May have had any number of prior systemic therapies for unresectable/metastatic disease.
e. Must have measurable or non-measurable disease as per RECIST 1.1
f. All patients with accessible tumor will be asked to provide a fresh tumor biopsy if they can be safely biopsied in the opinion of the investigator. Recently obtained archived core or excisional biopsy of a tumor lesion (obtained up to 12 months prior to Cycle 1 Day 1) may be substituted only if the patient is unwilling or unable (e.g. inaccessible or patient safety concern) to undergo a fresh tumor biopsy. Patients who are unwilling or unable to have a fresh tumor biopsy and do not have recently obtained archived tissue available may submit an archived specimen (obtained > 12 months prior to Cycle 1 Day 1) only upon approval from the Sponsor-Investigator.
g. Be ≥ 12 years of age on day of signing informed consent. Assent will be obtained in appropriately aged patients per institutional guidelines.
h. ECOG performance status 0 or 1.
i. Life expectancy of at least 3 months per the Investigator.
j. Have adequate organ function as indicated by the laboratory values in **Table 1 (below).** All screening labs should be performed within 10 days of study treatment initiation. PT/INR and PTT must be performed within 7 days of study treatment initiation for patients on anti-coagulants such as coumadin/heparin.
k. The patient has left ventricular ejection fraction (LVEF) ≥ 50% assessed within 21 days prior to study treatment initiation.
l. Patients must not be expecting to conceive or father children within the timeframe referenced below. Patients of childbearing potential must be willing to adhere to the contraception requirement as described in Section 3.3.2 from the day of the screening visit (or 14 days prior to the initiation of study treatment for oral contraception) throughout the study period up to 120 days after the last dose of pembrolizumab and/or up to 180 days after the last dose of doxorubicin. If there is any question that a patient of childbearing potential will not reliably comply with the requirements for contraception, that patient should not be entered into the study.
m. Female patients of childbearing potential must have a negative urine or serum pregnancy test at screening (within 72 hours of first dose of study treatment). If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required. The serum pregnancy test must be negative for the patient to be eligible.
n. Patient has voluntarily agreed to participate by giving written informed consent for the trial. The patient may also provide consent for Optional and Future Studies-Biospecimen Collection. However, the patient may participate in the main trial without participating in Optional and Future Studies.

Exclusion Criteria – Patients must not meet any of the following criteria
a. Currently participating and receiving study therapy or have participated in a study of an investigational agent and received study therapy or used an investigational device within 30 days of the first dose of study treatment.
b. Have a diagnosis of immunodeficiency or are receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of study treatment.
c. Have a known history of active TB (Bacillus Tuberculosis).
d. Have had a prior anti-cancer monoclonal antibody (mAb) given to treat malignancy within 4 weeks prior to the first dose of study treatment or have not recovered (i.e. ≤ Grade 1 or at baseline) from adverse events due to previous mAbs.
e. Have had prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to the first dose of study treatment or who have not recovered (i.e. ≤ Grade 1 or at baseline) from adverse events due to previous chemotherapy, targeted small molecule therapy, or radiation therapy. Note: Patients with ≤ Grade 2 neuropathy are an exception to this criterion and may qualify for the study. Note: If patients have received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study treatment as determined by the Investigator.
f. Have a known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin or squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer.
g. Have known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Patients with previously treated brain metastases may participate provided they are stable (without evidence of progression by imaging for at least four weeks prior to the first dose of study treatment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and are not using steroids for at least 7 days prior to the first dose of the study treatment. This exception does not include carcinomatous meningitis which is excluded regardless of clinical stability.
h. Have active autoimmune disease that has required systemic treatment in the past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g. thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
i. Have known history of, or any evidence of active, non-infectious pneumonitis.
j. Have an active infection requiring systemic therapy (uncomplicated urinary tract infection treated with oral antibiotics is permitted).
k. Have a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the patients' participation for the full duration of the trial, or is not in the best interest of the patients to participate, in the opinion of the treating Investigator.
l. Have known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial as determined by the Investigator.
m. Are pregnant or breastfeeding.
n. Have received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent.

o. Have a known history of Human Immunodeficiency Virus infection (e.g. HIV 1/2 antibodies).