Title: A Pilot Study to Evaluate Novel Agents (Temozolomide and Cixutumumab [IMC-A12, Anti-IGF-IR Monoclonal Antibody, IND #100947, NSC # 742460]) in Combination with Intensive Multi-Agent Interval Compressed Therapy for Patients with High-Risk Rhabdomyosarcoma (ARST08P1)

IRB# 2010-094
Principal Investigator: Carla Golden, MD

Synopsis:
This COG Pilot Study will evaluate novel agents (Temozolomide and Cixutumumab) in combination with intensive multi-agent interval compressed therapy for patients with high-risk rhabdomyosarcoma.

Patients with metastatic rhabdomyosarcoma (RMS) continue to have a poor prognosis with an overall survival rate of approximately 30%. Improvements in outcome for localized disease can be attributed to the use of intensive combination chemotherapy, better staging, more effective local therapy with surgery and radiation, as well as improved supportive care. However, these same strategies have failed to significantly improve the outcome for patients with metastatic RMS; thus an urgent need exists for novel approaches to therapy.

This protocol evaluates the addition of novel therapeutic agents to the intensive chemotherapy used in the COG study ARST0431. The study population will include select patients with metastatic RMS (excluding patients < 10 years of age with embryonal RMS) who have an expected failure-free survival of less than 20%. The sequential pilots proposed in this study assess three innovations.

- Pilot 1 assesses the feasibility of adding IMC-A12, a fully human IgG1 monoclonal antibody targeting the Insulin-like Growth Factor-I receptor (IGF-IR) to most known effective chemotherapy agents in RMS.

- Pilot 2 assesses the feasibility of adding temozolomide, an alkylating agent, to vincristine/irinotecan cycles, based upon the synergistic activity of temozolomide when added to irinotecan.

- If both pilots are tolerable, then Pilot 3 will assess the feasibility of adding both agents to the ARST0431 backbone. To obtain preliminary efficacy data, enrollment will be expanded on the pilot regimen that is shown to be feasible and thus, most compelling for future study.