Supplemental Appendix A: Study Eligibility

Inclusion Criteria

1. Patients of any age must have histologically or cytologically confirmed embryonal or alveolar rhabdomyosarcoma (RMS) confirmed by the Laboratory of Pathology, NCI or by the Department of Pathology and Laboratory Medicine, CHLA.
2. Patients must have measurable disease as per RECIST (version 1.1).
3. Patients must be able to undergo appropriate imaging studies to monitor tumor response.
4. Archival tissue of tumors (slides or blocks (blocks preferred) must be available for analysis. If tissue is not available, patients willing to undergo a pre-treatment biopsy may enroll.
5. Prior Therapies:
   i. There is no maximum number of prior medical therapies.
   ii. There must be no curative or life prolonging treatments available.
   iii. Patients who have received other IGF-1R antibodies or inhibitors are eligible, as long as an appropriate washout period has elapsed (see below).
   iv. Participants must have had their last fraction of external beam radiation therapy that is local and palliative at least 2 weeks prior to enrollment (except for radiation therapy to the lungs as noted below) and had their last substantial bone marrow radiation at least 6 weeks prior to enrollment.
   v. Participants must have had their last radiation therapy of the lungs at least 8 weeks prior to enrollment.
   vi. Participants must have had their last dose of temozolomide at least 4 weeks prior to enrollment; their last dose of other cytotoxic chemotherapy at least 3 weeks prior to enrollment; their last dose of biological therapy, such as biological response modifiers (e.g., cytokines), immunomodulatory agents, vaccines, differentiating agents, used to treat their cancer at least 7 days prior to enrollment, their last dose of a monoclonal antibody the shorter of 3 half- lives or 28 days prior to enrollment, and their last dose of any investigational agent at least 4 weeks prior to enrollment.
   vii. Participants must have recovered from the acute toxic effects of prior therapy to a grade 1 (CTCAE v.5.0) level prior to enrollment (does not apply to alopecia).
   viii. Age. There are no age limits for this study, but patients must have the ability to swallow tablets.
   ix. ECOG performance status ≤2 or Karnofsky ≥50% (if ≥ 16 years of age); or children < 16 years old must have a Lansky performance of ≥50%
   x. Patients must have normal organ and marrow function as defined below:
   i. Absolute neutrophil count ≥1,000/mcL
   ii. Platelets ≥75,000/mcL
   iii. Total bilirubin ≤1.5X upper limit of normal (ULN), with exception of patients with Gilbert syndrome
   iv. ALT ≤ 3.0X ULN
   v. Creatinine within normal institutional limits OR creatinine clearance ≥60 mL/min/1.73 m2 for patients with creatinine levels above institutional normal.
   vi. Normal blood glucose for age

9. Hematologic parameters for patients undergoing biopsy only: Patients should have INR <1.4 and PTT ≤ 40 seconds (unless due to lupus anticoagulant). In patients not meeting these parameters, clearance by hematology will be required prior to undergoing a biopsy.
10. Cardiac Function: QTcF < 480 msec (Fridericia correction), and ejection fraction (EF) ≥ 50%
11. Contraception: The effects of these agents on the developing human fetus are unknown. For this reason, men and women of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry, for the duration of study participation, and for 4 months after completion of administration of either agent. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately. Negative pregnancy test is required for women of childbearing potential.
12. Ability of subject or Legally Authorized Representative (LAR) to understand and the willingness to sign a written informed consent document.
13. Patients will be strongly encouraged to participate in 10-C-0086. If a patient does not agree to enroll on 10-C-0086, germline genetic analysis will not be performed.

Exclusion Criteria

1. Patients who are receiving any other investigational agents.
2. Patients with known brain metastases should be excluded from this clinical trial because of their poor prognosis and because they often develop progressive neurologic dysfunction that would confound the evaluation of neurologic and other adverse events.
3. History of allergic reactions attributed to compounds of similar chemical or biologic composition to dasatinib or ganitumab or other agents used in study.
4. Patients who require concurrent treatment with any medications or substances that are potent inhibitors or inducers of CYP3A4 are ineligible.
5. Patients who require concurrent treatment with antithrombotic and/or anti-platelet agents (e.g., warfarin, heparin, low molecular weight heparin, aspirin, and/or ibuprofen).
6. Patients with any condition (e.g., gastrointestinal tract disease resulting in an inability to take oral medication or a requirement for IV alimentation, prior surgical procedures affecting absorption, or active peptic ulcer disease) that impairs their ability to swallow and retain dasatinib tablets are excluded.
7. Patients with a history of radiation pneumonitis.
8. Patients may not have any clinically significant cardiovascular disease including the following:
   i. Myocardial infarction or ventricular tachyarrhythmia within 6 months
   ii. Major conduction abnormality (unless a cardiac pacemaker is present).

   Patients with any cardiopulmonary symptoms of unknown cause (e.g., shortness of breath, chest pain, etc.) should be evaluated by a baseline echocardiogram with or without stress test as needed in addition to electrocardiogram (EKG) to rule out QTc prolongation. The patient may be referred to a cardiologist at the discretion of the principal investigator. Patients with underlying cardiopulmonary dysfunction should be excluded from the study.
9. Uncontrolled intercurrent illness including, but not limited to, the following: ongoing or active infection; history of significant bleeding disorder, including congenital (von

Willebrand's disease) or acquired (anti-factor VIII antibodies) disorders; large pleural effusions; or psychiatric illness/social situations that would limit compliance with study requirements.

10. Patients with known pre-existing diabetes mellitus will be excluded because of the risk of hyperglycemia with ganitumab.
11. Pregnant women are excluded from this study because animal studies with dasatinib have shown embryolethality and fetal skeletal alterations at non-toxic maternal doses. Because there is an unknown but potential risk for adverse events in nursing human infants secondary to treatment of the mother with dasatinib, breastfeeding should be discontinued if the mother is treated with dasatinib.

Supplemental Appendix B: Dosing nomogram for dasatinib

Dose level																			
2 (60 mg/m^2/dose BID)	BSA*	0.5-0.54	0.55-0.62	0.63-0.71	0.72-0.79	0.8-0.87	0.88-0.96	0.97-1.04	1.05-1.12	≥1.13									
	Dose†	30	35	40	45	50	55	60	65	70									
1 (60 mg/m^2/dose once daily)	BSA*	0.5-0.54	0.55-0.62	0.63-0.71	0.72-0.79	0.8-0.87	0.88-0.96	0.97-1.04	1.05-1.12	1.13-1.21	1.22-1.29	1.3-1.37	1.38-1.46	1.47-1.54	1.55-1.62	≥1.63			
	Dose†	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100			
-1 (40 mg/m^2/dose once daily)	BSA*	0.5-0.56	0.57-0.69	0.70-0.81	0.8-0.94	0.95-1.06	1.07-1.19	1.2-1.31	1.3-1.44	1.45-1.56	1.57-1.69	1.7-1.81	1.82-1.94	1.95-2.06	2.07-2.18	2.19-2.31	2.32-2.44	≥2.45	
	Dose†	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100	

- *BSA, body surface area in m^2.
- †Actual dose in mg (tablet sizes 5 mg, 20 mg, and 50 mg).

Supplemental Appendix C: Dasatinib dose modification for toxicities (daily dosing)

Current Dose (Daily)	Reduced Dose (Daily)	% Decrease
100 MG PER DOSE	70 MG PER DOSE	30
95 MG PER DOSE	65 MG PER DOSE	32
90 MG PER DOSE	65 MG PER DOSE	28
85 MG PER DOSE	60 MG PER DOSE	29
80 MG PER DOSE	55 MG PER DOSE	31
75 MG PER DOSE	50 MG PER DOSE	33
70 MG PER DOSE	50 MG PER DOSE	28
65 MG PER DOSE	45 MG PER DOSE	31
60 MG PER DOSE	40 MG PER DOSE	33
55 MG PER DOSE	40 MG PER DOSE	27
50 MG PER DOSE	35 MG PER DOSE	30
45 MG PER DOSE	30 MG PER DOSE	33
40 MG PER DOSE	40 MG PER DOSE ON M, W, TH, SAT, SUN	28
35 MG PER DOSE	25 MG PER DOSE	29
30 MG PER DOSE	20 MG PER DOSE	33
25 MG PER DOSE	20 MG PER DOSE ON M, TU, W, TH, F, SAT	31
20 MG PER DOSE	20 MG PER DOSE ON M, W, TH, SAT, SUN	28

Dasatinib dose modification for toxicities (twice daily dosing)

Current Dose (BID)	Reduced Dose (BID)	% Decrease
70 MG PER DOSE	50 MG PER DOSE	28
65 MG PER DOSE	45 MG PER DOSE	31
60 MG PER DOSE	40 MG PER DOSE	33
55 MG PER DOSE	40 MG PER DOSE	27
50 MG PER DOSE	35 MG PER DOSE	30
45 MG PER DOSE	30 MG PER DOSE	33
40 MG PER DOSE	40 MG PER DOSE ON M, W, TH, SAT, SUN	28
35 MG PER DOSE	25 MG PER DOSE	29
30 MG PER DOSE	20 MG PER DOSE	33
25 MG PER DOSE	20 MG PER DOSE ON M, TU, W, TH, F, SAT	31
20 MG PER DOSE	20 MG PER DOSE ON M, W, TH, SAT, SUN	28