Table S3 Supplementary Material
Study Stopping Criteria[Δ]

Threshold	Events
General, target or vital organs related findings (in ≥ 2 subjects)	• Clinically relevant signs or symptoms, which in the opinion of the investigator warrant stopping of dose administration. • Tachycardia defined as HR ≥ 115 bpm over at least 30 minutes in supine position (HR measured by 12-lead ECG). • Absolute QTcF increases to >500 ms or QTcF increases >60 ms compared to baseline (based on an average QTcF value of triplicate ECGs). • Evidence of clinically significant increases in liver functions tests (ALT ≥ or AST≥ 2.5 x ULN and total bilirubin ≥ 1.5 x ULN). • A glomerular filtration rate (GFR) ≤90 mL/min/1.73m^2, or serum creatinine >2 mg/dL and >0.5 mg/dL increase from baseline value.
Gastrointestinal findings (in ≥ 4 subjects)	• Moderate nausea or vomiting on 3 (or more) occasions on 2 successive days leaving the subject unable to eat a meal (CTCAE ≥2). • Moderate diarrhoea defined as increase to 4 (or more) episodes per day over baseline (CTCAE grade ≥ 2).
Occurrence (in ≥1 subjects)	• The highest dose intended for administration as defined in this protocol has been reached.[‡] • ETC-206 total mean AUC $_{0\text{-inf}}$ of 7,230ng*h/mL or C_{max} of 935 ng/mL has been achieved (according to NOAEL observed in dogs at the dose of 3 mg/kg/day in the 4- week study).[‡] • Any other event that in the opinion of the sponsor and principal investigator warrant stopping of dose administration

Legend - CTCAE: Common Terminology Criteria for Adverse Events; NOAEL: No observed adverse effect level; [Δ]: Individual items work also as subject withdrawal criteria; [‡]: Removed with amendment after 10 mg SD administration in fasted condition.