

Supplementary Table S5—Adverse events observed during daily animal observations over 4 weeks of dosing for the dogs of Table S1.

Category	AE	Weeks observed	Placebo		1 mg/kg		2 mg/kg		4 mg/kg		12 mg/kg	
			AEs (n)	dogs (n)	AEs (n)	dogs (n)	AEs (n)	dogs (n)	AEs (n)	dogs (n)	AEs (n)	dogs (n)
GI	Hypersalivation	1, 2, 3, 4	-	-	-	-	-	-	1	1	20*	2*
	Lip-licking	1	3	3	-	-	1	1	2	2	2	1
	Vomiting	1, 2, 3, 4	2	1-2 [†]	1	1	4	2-4 [†]	2	1-2 [†]	4	1-2 [†]
	Dehydration (tacky mucous membranes)	4	-	-	-	-	-	-	-	-	1	1
	Loose Stool	1, 2, 3, 4	1	1	5	1-4 [†]	2	1-2 [†]	1	1	4	1-4 [†]
Non-GI												
Ocular	Protrusion membrana nictitans	1	1	1	-	-	-	-	-	-	-	-
Neurological	Ataxia [‡]	1	2	2	2	2	-	-	2	2	1	1
	Trembling or shaking	3, 4	-	-	-	-	-	-	-	-	2	1
	Hyperaesthesia	1	1	1	-	-	-	-	-	-	-	-
Constitutional	Lethargy [‡]	1, 4	1	1	2	2	1	1	1	1	1	1
Respiratory	Tachypnoea	3	-	-	-	-	-	-	-	-	1	1

n, number

*Indicates 20 total occurrences of hypersalivation across two dogs (not 20 observations in each of two dogs) over four weeks of dosing. Only the first occurrence on a particular day was counted for a subject.

[†] Dogs in a treatment group were socialized and housed together. Upon the first observation of an episode of vomiting or loose stool, the dogs were subsequently individually housed for close monitoring. A range is reported in some cases to account for the uncertainty of whether episodes occurring during group housing/socialization were in the same dogs that experienced the episode during individual housing.

[‡] Criterion for ataxia was “wobbles on feet but able to correct balance”. All seven episodes of ataxia and five of six episodes of lethargy occurred on the first day of dosing. Of the seven dogs who experienced ataxia, four of them were also observed to be lethargic. A plausible explanation for ataxia and lethargy is fatigue as a result of study procedures, such as multiple blood draws for PK profiles.