Supplementary Appendix S1—Cannabidiol Assay: Cannabidiol (CBD) was measured in canine plasma using a validated LC/MS/MS assay carried out in the Pharmacology Laboratory of the Drug Development & Discovery Shared Resource (University of Colorado Cancer Center). The instrumentation included an Applied Biosystems 3200 Q-TRAP triple quadrupole mass spectrometer coupled to a Shimadzu LC20AD and HTC-PAL autosampler. Unknown and quality control (QC) samples were prepared by adding known amounts of CBD (1-1000 ng/ml) into 100 µl blank plasma in a volume of 10 µl prepared in 50/50 acetonitrile and MilliQ H_2O. Samples (unknowns, standards, and QCs) were prepared for analysis by adding 10 µl d3-CBD (100 ng/ml, internal standard) and 10 µl 50/50 acetonitrile and MilliQ H_2O to unknown samples, followed by 600 µl cyclohexane, vortex mixing for 5 minutes, and then centrifuged for 10 minutes at *13,300 rcf* and 500 µl of the resulting supernatant collected and transferred a microcentrifuge tube and evaporated to dryness using a rotary evaporator. The samples were the resuspended in 100 µl of 50/50 acetonitrile and MilliQ H_2O and transferred to sample vials with a low volume insert. Sample injection volume was 30 µl (using a 20 µl loading loop) and chromatography was carried out using a Waters Sunfire C18 5µm column (4.6 x 50 mm) and a solvent system consisting of acetonitrile with 0.1% formic acid (solvent A) and Milli-Q water with 0.1% formic acid (solvent B). CBD and d3-CBD (internal standard) were eluted using a gradient starting at 70% solvent A:30% solvent B for the first 1.5 minutes and then transitioning linearly to 99% solvent A:1% solvent B over a 2.5 minute period and holding until 5 minutes when the original 70% solvent A:30% solvent B was re-established over a 1.0 minute period and held for the remainder of the 7.0 minute total run time. The mass spectrometer was operated in positive ion mode with an ion spray voltage of 5500 V and a source temperature of 550ºC. Multiple reaction monitoring (MRM) analysis was carried out for CBD by monitoring ion transitions of 315.2 *m/z* → 193.3 *m/z* and 315.2 *m/z* → 259.5 *m/z* and for d3-CBD at 318.1 *m/z* → 196.3 *m/z*. MRM conditions were optimized using internal algorithms

and both Q1 and Q3 were operated at unit resolution. Assay performance was monitored using QC samples at 3 levels (5, 50, and 500 ng/ml) and showed an accuracy and precision (%CV) of 90.0% ± 8.4% across 3 batches with 32/36 QC's passing with greater than 85% accuracy and a lower limit of quantitation of 2.5 ng/ml.