



Supplemental Figure 1. Time-concentration profiles of mGlu₅ PAMs demonstrate rapid absorption into the systemic circulation and brain. Male Sprague-Dawley rats received an i.p. dose of A) VU0360172, B) VU0361747 or C) VU0092273 at 10 mg/kg in 10% Tween 80. Concentrations of test compound were measured in systemic blood and whole-brain tissues 0.25, 0.5, 1, 3 and 6 hours following dosing. Data are expressed as mean \pm S.E.M of the plasma (ng/ml) or brain (ng/g) concentration (n = 2-3). D) Summary of maximum brain concentration (C_{max}) and time (T_{max}), in addition to free fraction (f_u) of test compounds as determined by brain homogenate binding. n.d. values not determined.