



**SUPPLEMENTARY FIG. S2.** Physiological monitoring of animals revealed no adverse effects during surgery or weight change with drug treatment. Representative pulse oximetry readings of heart rate and arterial oxygenation for sham (**A,B**) and traumatic brain injury (TBI) (**C,D**) animals, respectively, with the accepted normal range depicted. Red arrows indicate (from left to right): surgery initiation, craniotomy, controlled cortical impact (CCI) (C-D only), and end of surgery. (**E**) Mean measures for heart rate (graphed at 1/4<sup>th</sup> scale), breath rate, and arterial oxygen across sham and TBI injured animals, reported as mean  $\pm$  standard error of the mean (SEM), with no significant differences. (**F**) Trend in animal weight across the first four days post-CCI, normalized to pre-injury measures, showing no significant weight loss after TBI with CLP290 or vehicle administration, reported as mean  $\pm$  SEM normalized to sham-vehicle control, with no significant difference.