Supplementary Figure 1: Effect of preventative L-006235 (30mg/kg) on MIA-induced weight bearing asymmetry (A) and log transformed ipsilateral hindpaw withdrawal thresholds (B). Group sizes were as follows: saline + vehicle, n = 5; MIA + vehicle, n=9; MIA + L-006325, n =10. Data were analysed by two way ANOVA with Bonferroni corrected multiple comparisons: ****p<0.0001, ***p<0.001, **p<0.01 MIA-Vehicle versus Saline-Vehicle. ####p<0.0001, ###p<0.001, ##p<0.01, #p<0.05 MIA-Vehicle versus MIA-L-006325. Data are presented as mean±SEM.
Supplementary Figure 2: Representative images of the joint pathology of rats following preventative treatment with L-006235. Images taken with a Zeiss Axiocam MRc camera. A) Changes in chondropathy in the medial tibial plateau. B) Synovitis. C) Quantification of CD68 positive cells in the synovium of rats injected with saline (n=6), MIA + vehicle (n=10), and MIA + L-006235 (100mg/kg) (n=8) on day 27. No significant difference between groups. D) Quantification of CD206 positive cells in the synovium of rats injected with saline (n=6), MIA + vehicle (n=10), and MIA + L-006235 (100mg/kg) (n=8). No significant difference between groups. Data are presented as mean ± SEM.
Supplementary Figure 3: A) Relative expression of cathepsin K mRNA in the ipsilateral dorsal quadrant of spinal cords taken from male Sprague Dawley rats 28 days post MIA (n=6) or saline (n=6) injection. There was no significant difference between the two groups (unpaired t-test). B) Preventative treatment with 100mg/kg L-006235 (n= 6) did not significantly alter GFAP immunoreactivity in the dorsal horn of the spinal cord, compared to vehicle treated animals (n=7) 27 days after intra-articular injection of MIA. Data are presented as mean ± SEM.
Supplementary Figure 4: Effects of L-006235 (100mg/kg) on ipsilateral hindpaw withdrawal thresholds (Study 3). 14 days after intra-articular injection of MIA rats received oral dosing of vehicle or L-006235 (100mg/kg) twice daily until day 40. Data are presented as a timecourse of log transformed paw withdrawal values. Group sizes were: MIA + vehicle, n=10; MIA + L-006235, n=10. Data were analysed with a two-way ANOVA with Bonferroni corrected multiple comparisons and no significant difference was found between groups at any timepoint. Data are presented as mean±SEM.
Supplementary Figure 5: Representative images of the joint pathology of rats following therapeutic treatment with L-006235. Images taken with a Zeiss Axiocam MRc camera. A) Chondropathy in the medial tibial plateau. B) Synovitis.