Supplementary Figures & Figure Legends:



Supplemental Figure1: Effect of K118 treatment on energy expenditure of Chow fed lean mice:CLAMS analysis using individually housed groups K118 and vehicle administered chow fed lean mice after two weeks of treatment. Plots represent variations in oxygen consumption (A), CO_2 release (B) and energy expenditure (C) over time in vehicle vs K118 treated mice (n=8) as indicated. Statistical analysis was performed using two-tail ratio paired T-test. Error bars are the mean \pm SEM.***P*<0.001, *****P*<0.0001



Supplemental Figure2: Effect of K118 treatment on ILC2, eosinophil & MDSC

A. SVF of WAT of 2 weeks K118 or vehicle treated mice stimulated with PMA (40ng/ml), ionomycin (500ng/ml) and brefeldin A for 4 h. Flow cytometry plots showing IL5 & IL13 production in ILC2 cells (Lin⁻CD45⁺CD4⁻IL7R α ⁺ST2⁺).**B**. Eosinophil gating strategy as described previously.(6). C-D pAKT phosphorylation in Eosinophils (C) and MDSC (D) by flow cytometry. Student's t-test, *P < 0.05, **P < 0.01E.Flow cytometry plots indicating gating strategy of M1 & M2 described macrophages elsewhere. M1 as (CD19⁻CD11b⁺F4/80⁺GR1^{Dim/-}CD11c⁺CD86^{Dim)}, M2 (CD19⁻CD11b⁺F4/80^{+m}GR1^{Dim/-}CD11c⁻ ^{/Dim}CD86⁺(18)





Supplemental Figure 3: Long-term K118 treatment in mice does not adversely impact any tissue or bone integrity.

(A-F) Histological appearance of tissues harvested from DIO mice treated with K118 (10mg/kg body weight) or vehicle for four weeks (2x/week). Tissues of K118-administered mice, including

(A) kidney, (B) liver, (C) lung, (D) spleen, (E) small intestine, and (F) large intestine were without significant abnormalities and comparable in appearance to those of vehicle-administered mice (H&E, 100X). (G-H) Bone mineral density (BMD) (G) and bone mineral content (BMC) (H), before (Pre-Tx) and after K118 and vehicle treatment. All results are expressed as mean \pm *SEM, Student's unpaired, two-tailed t test *p* \leq 0.05, (n=6).