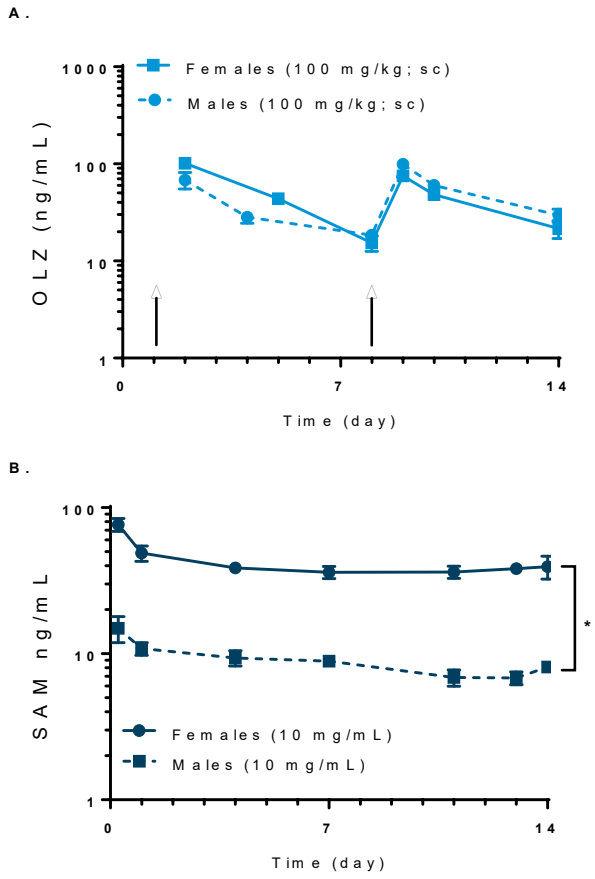
Supplemental Data

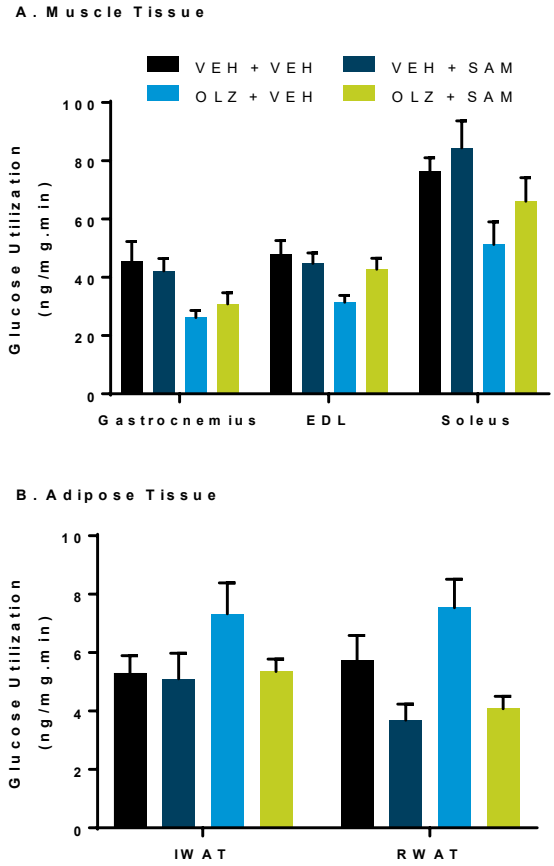
Supplemental Data Figure 1



Pilot PK studies

Based on clinical C_{max} steady state plasma levels of ALKS 3831 (Sun et al., 2018), pilot studies were designed to target clinically relevant plasma concentrations of OLZ and SAM in rodents. A. The dose of OLZ (100 mg/kg) was chosen based on previously reports which delivered clinically relevant and stable concentrations in female rats (Skrede et al., 2014). Average steady state values under these conditions were (mean ± SEM) 51.0 ± 12.6 mg/mL and 50.7 ng/mL ± 13.4 for females and males, respectively. Importantly as determined by an unpaired two-tailed t test, there were no differences in average plasma concentrations between female and male rats (($t_{(10)} = 0.02$, $p = 0.99$). B. Female and male rats were implanted with Alzet® osmotic mini pumps (model 2ML2; 5 uL/hr) filled with 10 mg/mL of SAM. Steady state concentrations achieved were 44.8 ng/mL ± 5.2 and 9.4 ± 1.1 ng/mL for females and males, respectively and average concentration of SAM in males was significantly lower compared to females ($t_{(12)} = 6.31$, $p < 0.0001$). The results of these studies were used to extrapolate the pump concentrations of SAM used in future experiments. Arrows indicate time of OLZ injection.

Supplemental Data Figure 2



Tissue-specific glucose utilization

A. Glucose utilization for gastrocnemius, extensor digitorum longus (EDL) and soleus muscle tissues. B. Glucose utilization for inguinal (iWAT) and retroperitoneal (rWAT) adipose tissues. The net effect of OLZ, SAM alone and in combination are analyzed and shown in figure 4 in the manuscript. Data are expressed as mean ± (SEM)