Supporting Information

[1,2,5]oxadiazolo[3,4-*b*]pyrazine-5,6-diamine Derivatives as Mitochondrial Uncouplers Towards Potential Treatment of Nonalcoholic Steatohepatitis

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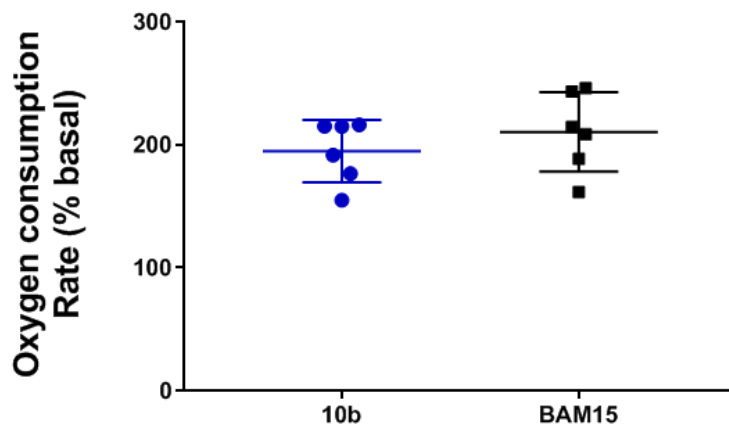Corresponding Author Email: santosw@vt.edu; k.hoehn@unsw.edu.au

Figure S1. Compound 10b is bioactive in rat primary hepatocytes. Rat primary hepatocytes treated with 1 µM **BAM15** or 1 µM compound **10b** increase cellular oxygen consumption rate by 2-fold in rat primary hepatocytes.
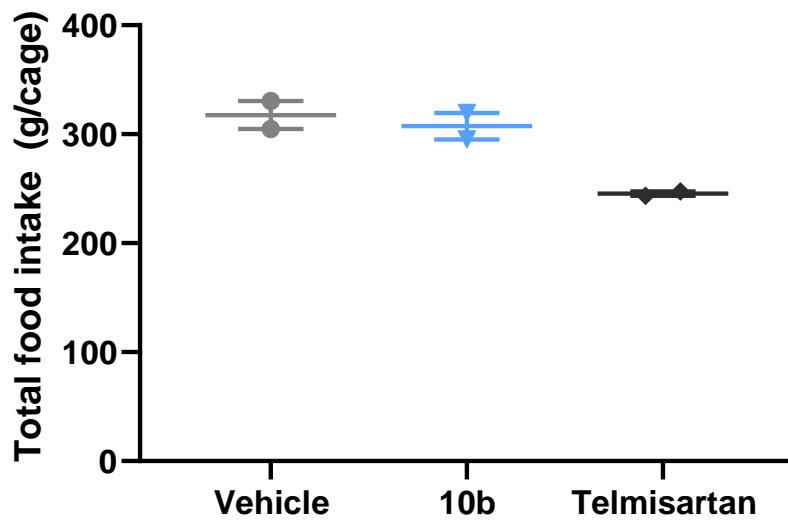
Figure S2. Total food intake measured per cage over the duration of the STAM study. n=2 cages per group.
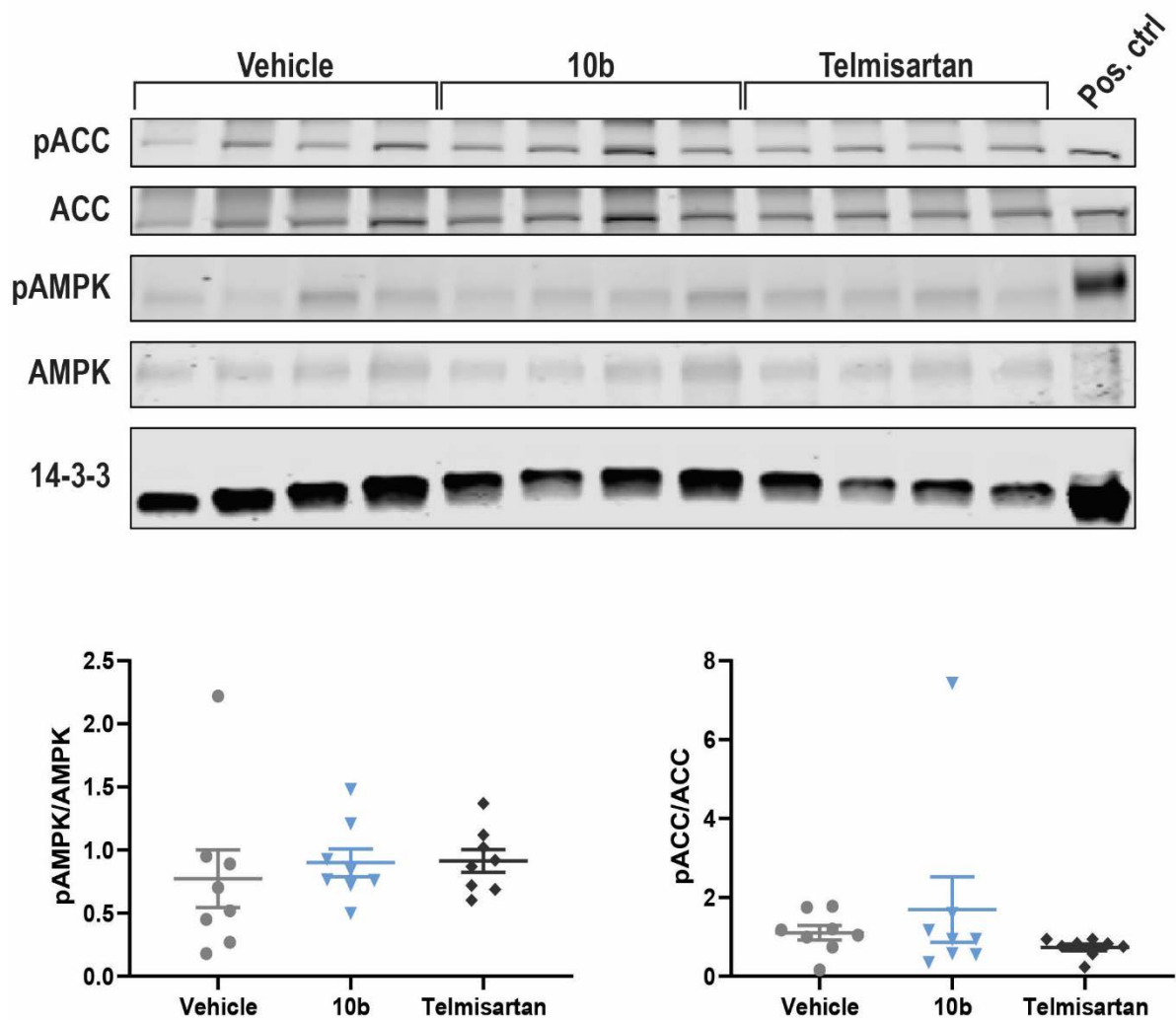
Figure S3. AMPK is not activated in liver tissue of mice treated with 10b in the STAM model.
Liver tissue from mice in each treatment group were assessed for phosphorylated and total ACC and AMPK by western blot. Normal murine liver cells treated with 5 μM FCCP for 1 hour were included as a positive control for AMPK activation. Densitometry was performed on samples from n=8 male mice per group. Statistical significance was assessed by Kruskal-Wallis test with Dunn's correction for multiple comparisons for non-parametric data.
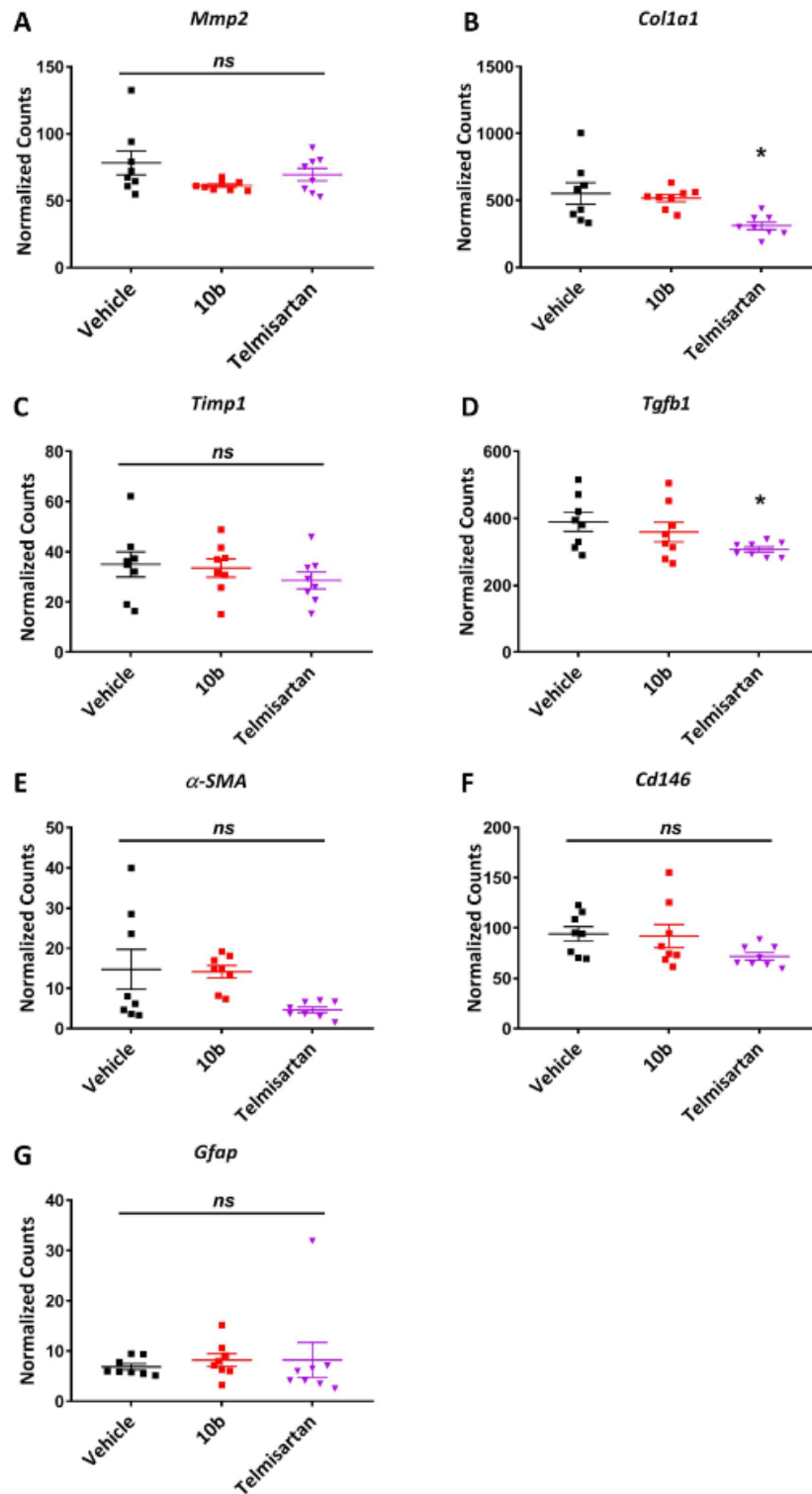
Figure S4. 10b and telmisartan effects on liver fibrosis marker gene expression. Liver tissue was evaluated for mRNA expression of A) matrix metallopeptidase 2 (*Mmp2*), B) tissue inhibitor matrix metalloproteinase 1 (*Timp1*), C) collagen 1A1 (*Col1a1*); D) transforming growth factor β1 (*Tgfb1*), E) alpha-smooth muscle actin (*a-SMA*), F) cluster of differentiation 146 (*Cd146*), and G) glial fibrillary acidic protein (*Gfap*). Results are shown as mean -/+ SEM with one-way ANOVA and Dunnett's post-hoc test. *p<0.05 vs vehicle.