Figure S1. Body weights pre- and post-treatment. A) Experimental timeline. Mice were injected at 5 weeks of age (week 0 of experiment) with tamoxifen to induce deletion of *Thm1*. Mice were fed *ad libitum* from 0-10 weeks post-tamoxifen injection to obtain the obese phenotype in *Thm1* cko mice. At week 10 (10 weeks post-tamoxifen injection), mice were housed individually and food intake and body weight were measured daily. From week 11-13, subcutaneous injections of ZGN-1258 or vehicle were administered daily. **B)** Body weights at week 10; **C)** week 11 **D)** Percent body weight change during week 10. Statistical significance was determined by two-tailed t-test. **E)** Body weights at week 13. Bars represent mean ± SD. Statistical significance was determined by one-way ANOVA followed by Tukey's test. Each data point represents an individual mouse. *P<0.05; ***P<0.0005; ****P<0.00005
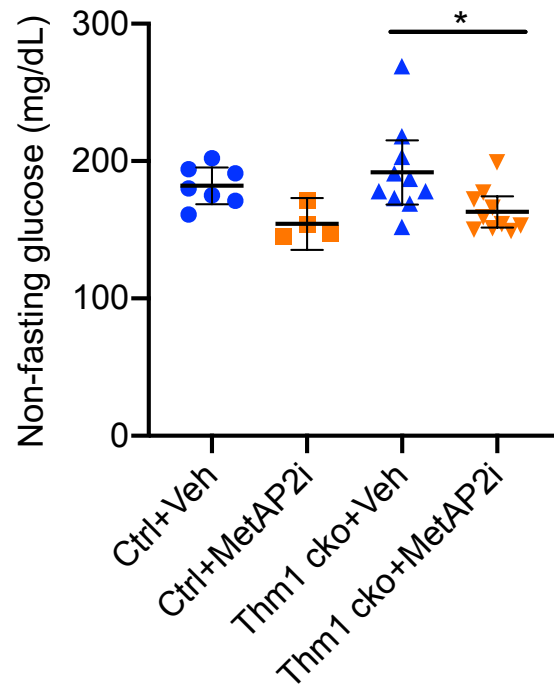
Figure S2. Non-fasting levels of serum glucose. Each data point represents an individual mouse. Bars represent mean ± SD. Statistical significance was determined by one-way ANOVA followed by Tukey's test. *P<0.05
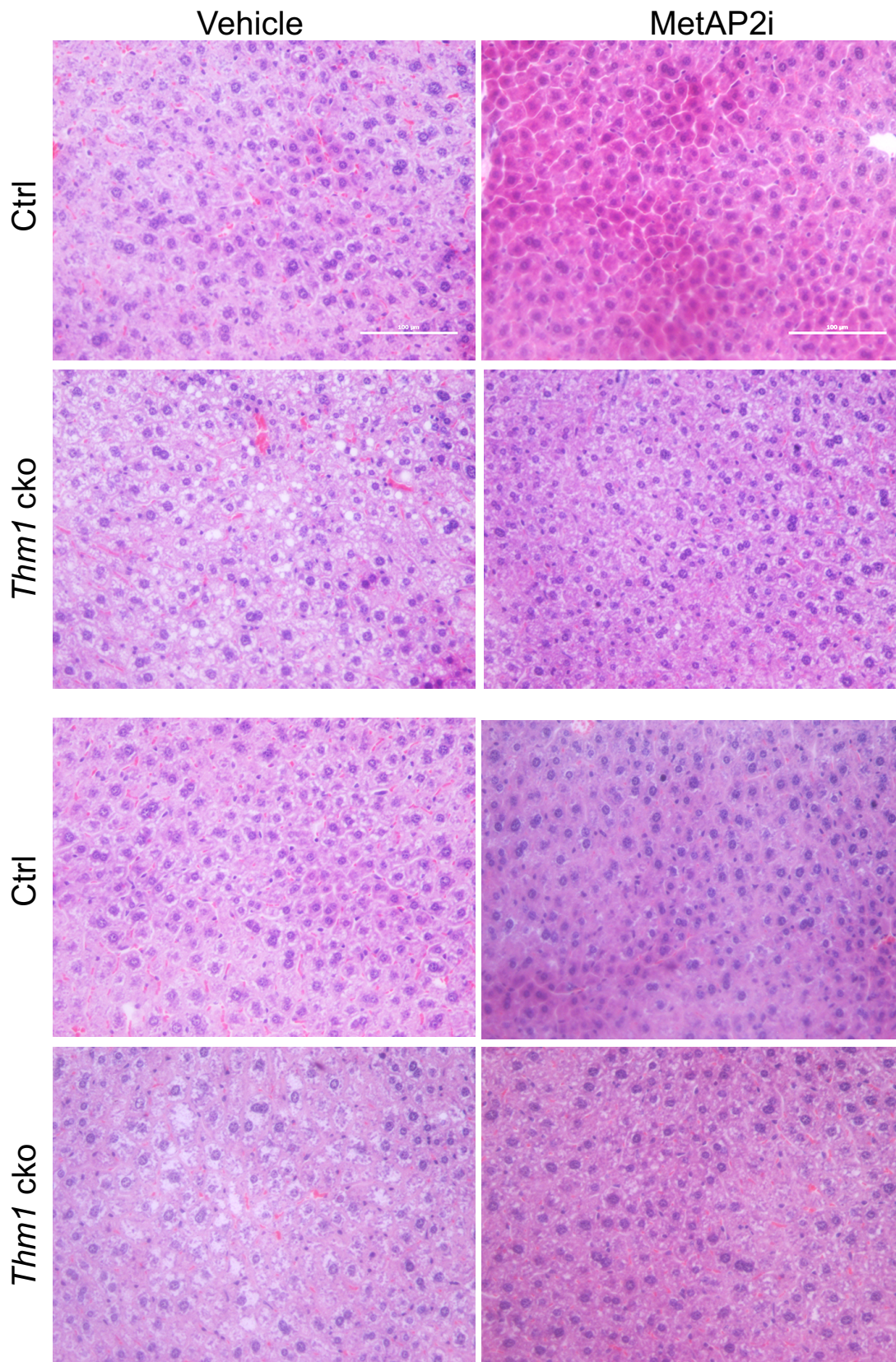
Figure S3. Improved liver morphology in MetAP2i-treated *Thm1* cko mice. Liver histology of vehicle and MetAP2i-treated control and *Thm1* cko littermates. N=2 litters. Scale bar - 100μm.
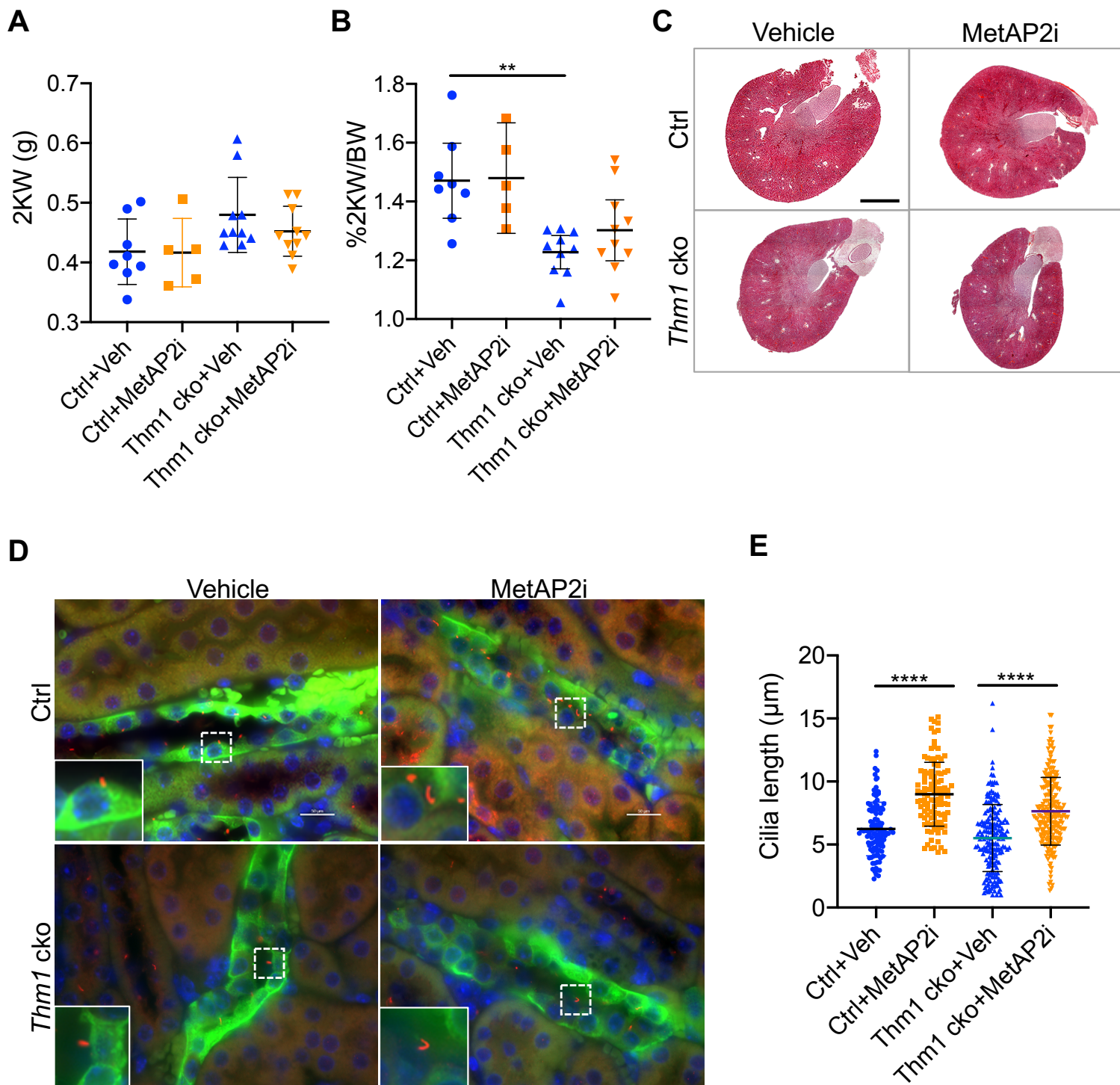
Figure S4. MetAP2i treatment increased renal cilia length. A) 2x kidney weight **B)** Percent 2x kidney weight/body weight. Each data point represents an individual mouse. **C)** Histology of kidneys of vehicle and MetAP2i treated control and *Thm1* cko mice. Scale bar- 1000μm **D)** Immunostaining of primary cilia membrane protein, ARL13B (red), together with staining with lectin DBA (green), which marks the collecting duct. Insets show higher magnification of dotted boxed regions. Scale bar – 50μm. **E)** Quantification of cilia length from N=3 mice/group. Each data point represents a cilium. Bars represent mean ± SD. Statistical significance was determined by one-way ANOVA followed by Tukey's test. **P<0.005; ****P<0.00005