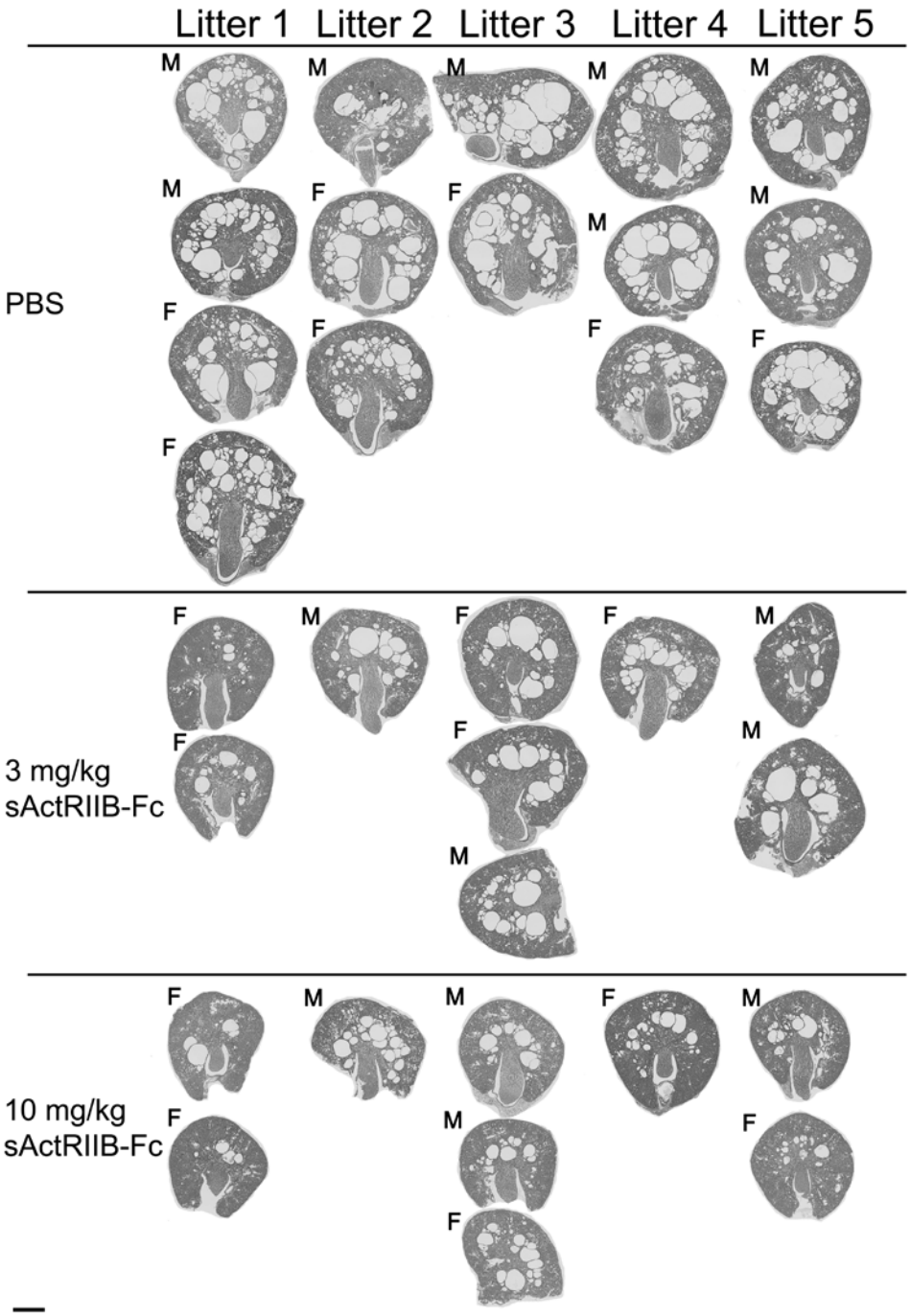
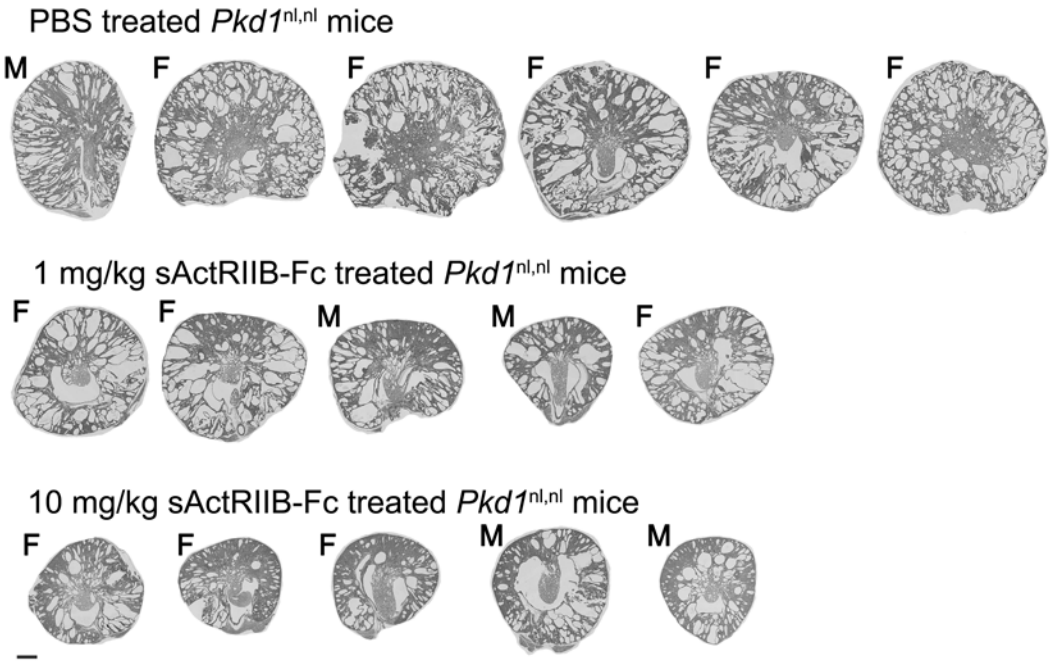
Supplemental Figure 1



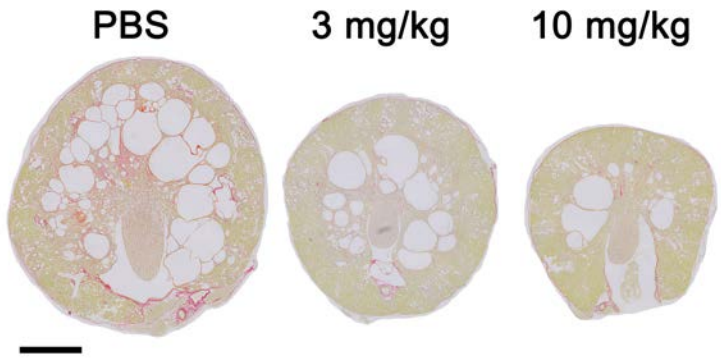
Supplemental Figure 1. Effect of sActRIIB-Fc on renal histology in *Pkd1*-cKO mice. Each litter was subdivided in a PBS, 3 mg/kg, or 10 mg/kg sActRIIB-Fc treatment group. Histology of all mice are shown. M; indicates male, F; indicates female. The mice on sActRIIB-Fc treatment had improved renal histology compared to the PBS treated mice.

Supplemental Figure 2



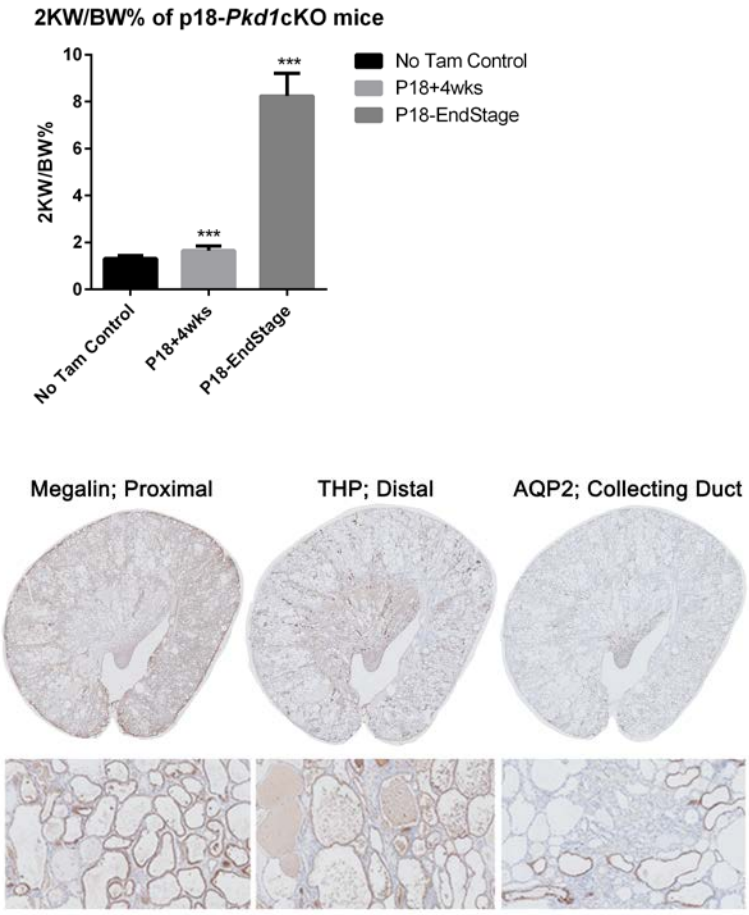
Supplemental Figure 2. Effect of sActRIIB-Fc on renal histology in *Pkd1*^{nl,nl} mice. The mice were treated 4 times between P10-P21 with either PBS alone, 1 mg/kg, or 10 mg/kg sActRIIB-Fc. Renal histology of all mice are shown. M; indicates male, F; indicates female. The kidneys from mice on sActRIIB-Fc were smaller and generally appeared less cystic compared to the kidneys of the PBS treated mice. Scale bar: 1 mm

Supplemental Figure 3



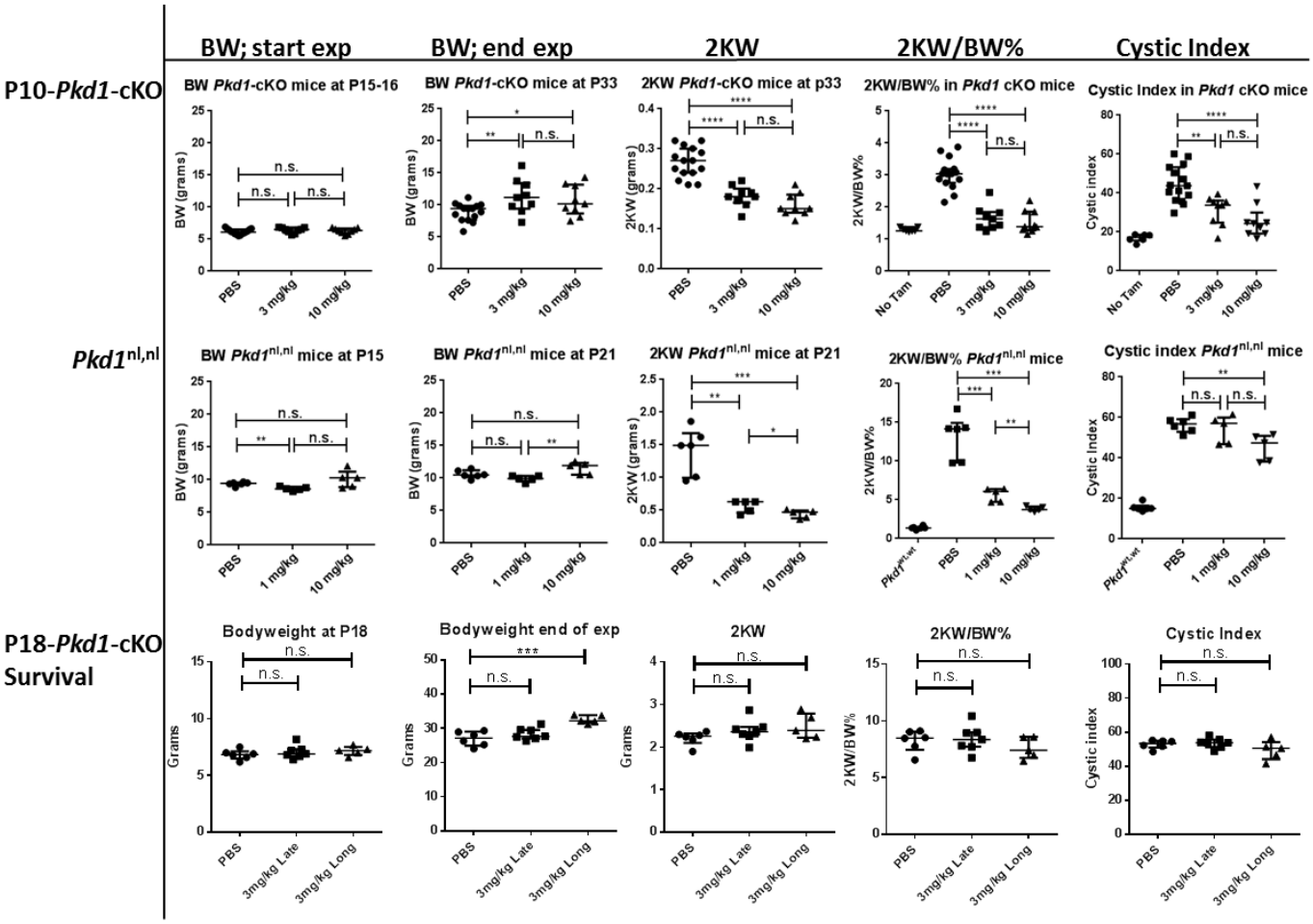
Supplemental Figure 3. Example images of SiriusRed stainings of renal sections of P10-*Pkd1*-cKO mice that were either treated with PBS, 3 mg/kg or 10 mg/kg sActRIIB-Fc. Quantification is shown in Figure 5C.

Supplemental Figure 4



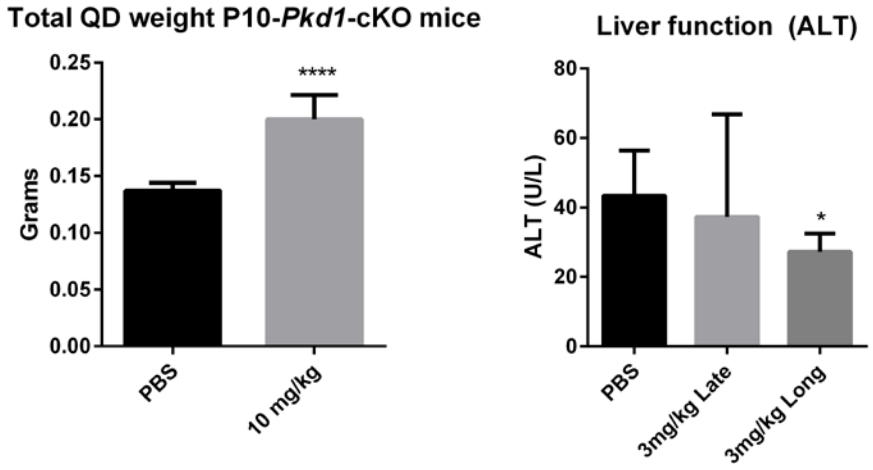
Supplemental Figure 4. Characteristics of the P18-*Pkd1*-cKO mouse model. *Pkd1*-cKO mice were treated with 150 mg/kg Tamoxifen or left untreated. At 4 weeks after Tamoxifen (n = 9 mice), the 2KW/BW% had increased slightly compared to control mice without Tamoxifen (n = 12 mice). The mice were then followed until the onset of renal failure (indicated as having a BU > 20 mmol/L; n = 6 mice), which occurred approximately at 100 days of age (see also Figure 6), with 2KW/BW% of approximately 8%. Segmental marker staining using anti-Megalin (proximal tubular marker), anti-Tammhorsfall protein (distal tubular marker), or Anti-Aqp2 antibodies (Collecting duct marker), revealed cyst formation from all tubular segments. Differences in 2KW/BW% between all groups: *** $P < 0.001$

Supplemental Figure 5



Supplemental Figure 5. Summary of bodyweight (BW) at the beginning and at the end of the experiment, of the total kidney weights (2KW) and of the 2KW/BW%, and of the cystic indices of all mice in this study is shown. Of note, the sActRIIB-Fc treated mice that were euthanized at fixed time points (the P10-*Pkd1*-cKO and the *Pkd1*^{nl,nl} mice) had lower kidney weights and lower cystic indices compared to their PBS treated littermates. The kidney weights and cystic indices were not different between the groups of the P18-*Pkd1*-cKO mice but the progression was slower in the sActRIIB-Fc treated mice compared to their PBS treated littermates (see Figure 6). * indicates $P < 0.05$, ** indicates $P < 0.01$, *** indicates $P < 0.001$, **** indicates $P < 0.0001$.). n.s. indicates Not significant

Supplemental Figure 6



Supplemental Figure 6. Additional effects of sActRIIB-Fc. The weight of the quadriceps's (QD) of sActRIIB-Fc treated P10-*Pkd1*-cKO mice (10 mg/kg) is higher than the QD weight of their PBS treated littermates. Alanine aminotransferase (ALT) blood levels were measured in the P18-*Pkd1*-cKO mice at the end of the experiment. Liver function was normal in all tested groups. * indicates $P < 0.05$, **** indicates $P < 0.0001$.