

**Supplemental Figure 1.** (A) Sclerostin mRNA expression in MDA-MB-231 metastatic breast cancer cells transfected with scrambled siRNA (Ctrl) or 3 different siRNAs (A, B, C) against sclerostin was quantified by qRT-PCR 24 and 48 hours after transfection (n=4). (B) Immunoblot analysis of sclerostin protein expression 24 and 48 hours after transfection with Control (Ctrl) or sclerostin siRNA. Data are represented as mean  $\pm$  SEM. Two groups were compared using 2-tailed Student's t-test, \*\*\*p<0.001.



Supplemental Figure 2. (A) Quantification of the metastases area in the femur of cancer-bearing mice treated with vehicle (n=8) or Scl-Ab (n=8) using histological sections. (B) Immuno-histochemistry of the human leukocyte antigen (HLA) in the lung and in the brain of cancer-bearing mice treated with vehicle or Scl-Ab. Representative images are shown. Scale bars indicate 50  $\mu$ m. Data are represented as mean ± SEM. Two groups were compared using 2-tailed Student's t-test, \*p<0.05.



**Supplemental Figure 3.** (A and B) Micro-computed tomography ( $\mu$ CT) images (A) and analysis (B) of the distal femur of healthy mice without treatment (n=5) and with vehicle (n=10) or Scl-Ab (n=10) treatment. (C and D)  $\mu$ CT images (C) and analysis (D) of the proximal tibia of healthy mice without treatment and with vehicle or Scl-Ab treatment. (E and F)  $\mu$ CT images (E) and analysis (F) of the cortical thickness of the midshaft femur of healthy mice without treatment and with vehicle or Scl-Ab treatment. BV/TV, bone volume/total volume; Tb.N, trabecular number; Tb.Th, trabecular thickness; Tb.Sp, trabecular separation; Ct.Th, cortical thickness. Data are represented as mean ± SEM. Three groups were compared using ANOVA followed by Tukey's post-hoc analysis, \*\*\*p<0.001.

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**Supplemental Figure 4.** (A) P1NP serum concentration of cancer-bearing mice treated with vehicle (n=8) or Scl-Ab (n=8). (B) Serum Tartrate-resistant acid phosphatase (TRAP) 5b concentration in cancer-bearing mice treated with vehicle (n=8) or Scl-Ab (n=8). (C) TRAP staining of the distal femur of cancer-bearing mice treated with vehicle (n=8) or Scl-Ab (n=8). Scale bar indicates 50  $\mu$ m. Data are represented as mean ± SEM. Two groups were compared using 2-tailed Student's t-test, \*p<0.05.





**Supplemental Figure 5.** (A) Immunoblot analysis of phosphorylated ERK1/2 (p-ERK1/2), total ERK1/2, phosphorylated STAT3 (p-STAT3) and total STAT3 in the *gastrocnemius* muscle of healthy non-treated mice (n=5) and in cancer-bearing mice treated with vehicle (n=8) or Scl-Ab (n=8). Actin was used as loading control. Representative images are shown. (B) Immunoblot analysis of phosphorylated p38 (p-38) and total p38 in C2C12 myoblasts stimulated with vehicle (veh) or recombinant sclerostin. Actin was used as a loading control. Representative images of 4 independent experiments are shown.