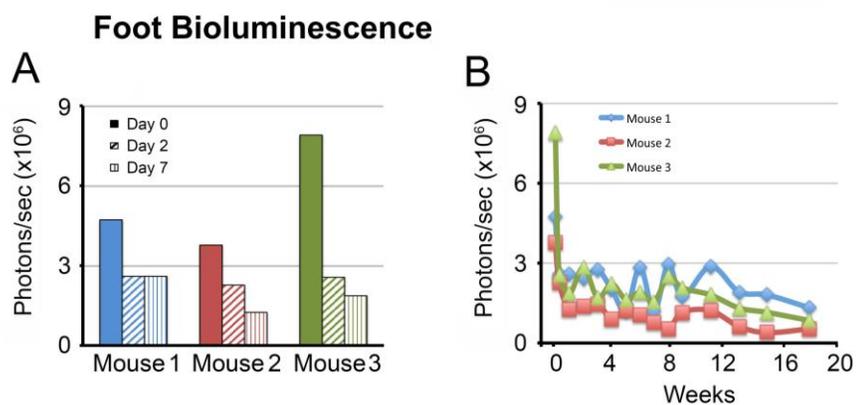
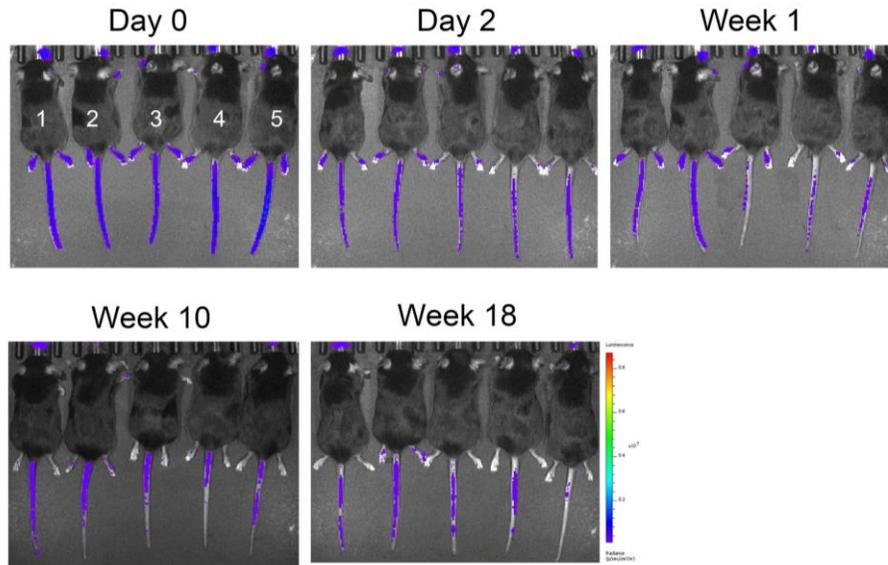


## Supplementary Figures and Figure Legends

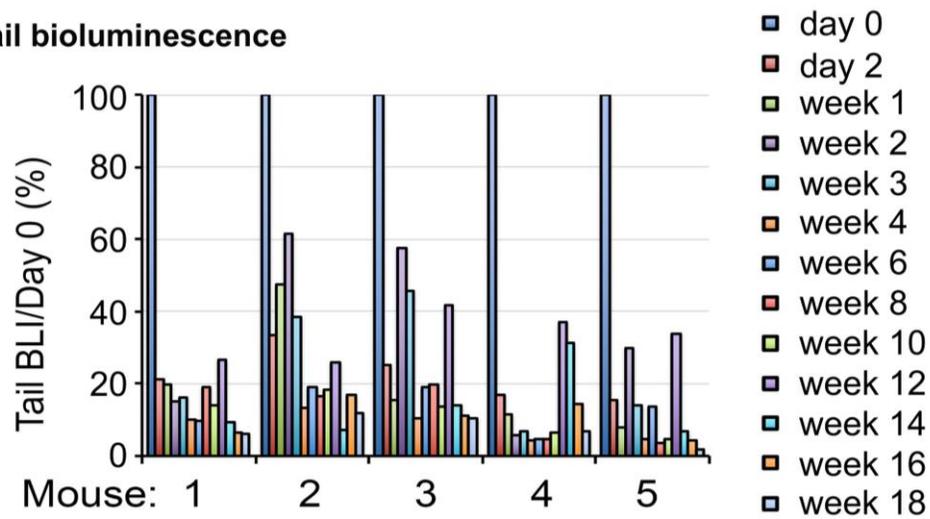


**Figure S1.** Ra-223 treatment decreases luciferase activity in the bones of mouse feet. Col-Luc/SCID mice were treated with 300 kBq/kg Ra-223, and the luciferase activity was monitored for 18 weeks using an IVIS 200 imaging system. (A) Photon counts of the feet of three Col-Luc/SCID mice right before Ra-223 injection (day 0) and on days 2 and 7. (B) Photon counts of mouse feet from 0 to 18 weeks.

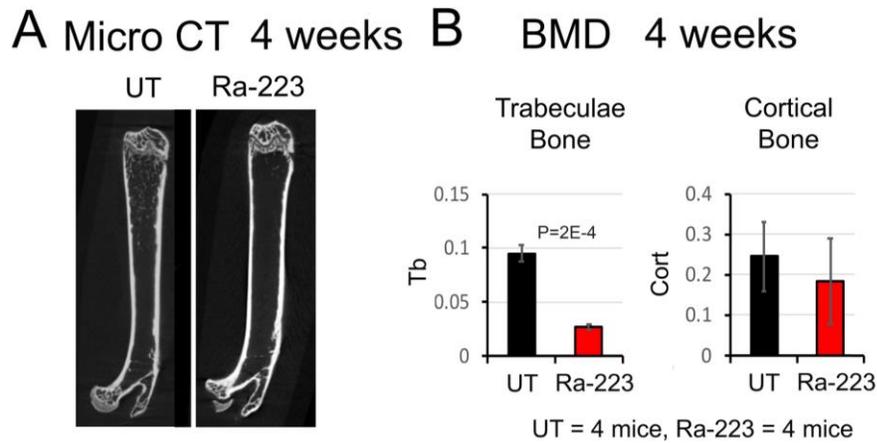
## A Bioluminescence of Col-Luc/B6 female mice



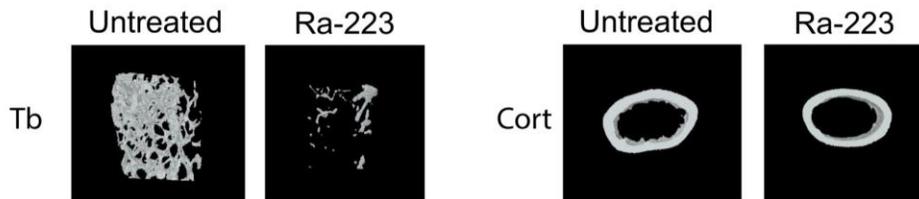
## B Tail bioluminescence



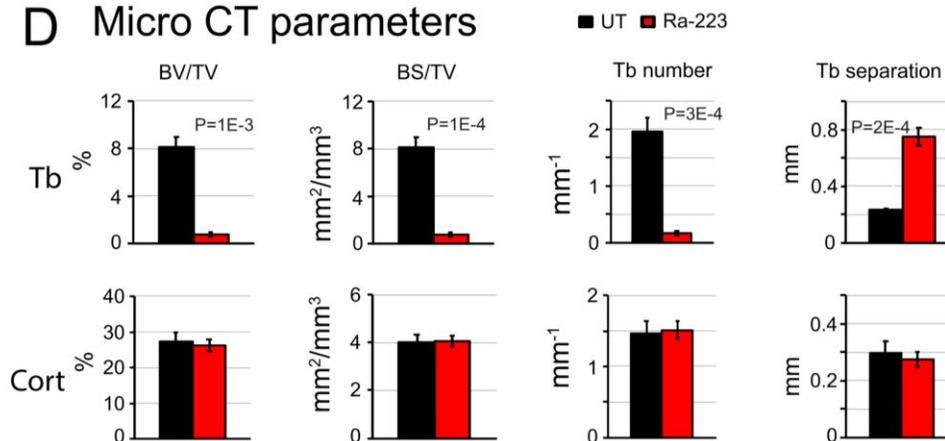
**Figure S2.** Ra-223 treatment decreases tail luciferase activity in female Col-Luc/B6 osteoblast reporter mice. Five female Col-Luc/B6 reporter mice were treated with a single dose of Ra-223 and monitored for 18 weeks. (A) BLI of mice. (B) Quantitation of tail photon counts over 18 weeks.



**C** 3D image

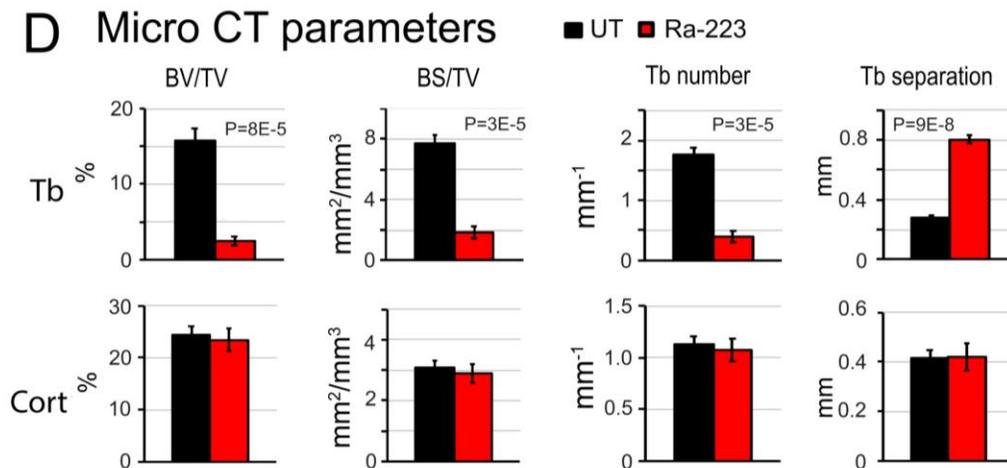
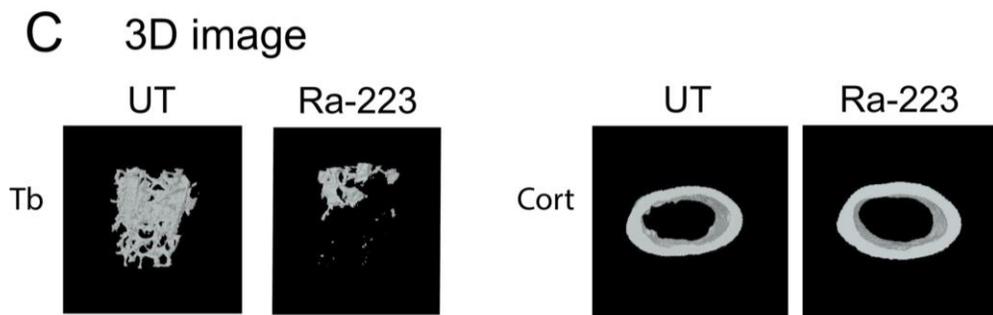
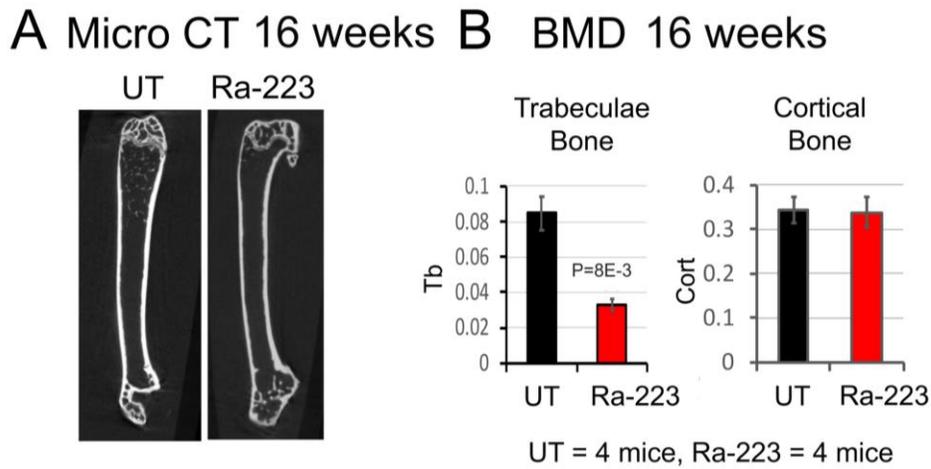


**D** Micro CT parameters



**Figure S3.** Ra-223 significantly decreased trabecular bone densities in female Col-GFP/B6 reporter mice 4 weeks after Ra-223 treatment. Eight 10-week-old female Col-GFP/B6 mice were used. Four mice were treated with one dose of Ra-223 at 300 kBq/kg, and the other four mice remained untreated (UT). Four weeks later, femurs of the mice were processed for micro-computed tomography ( $\mu$ CT) analysis. (A) Representative  $\mu$ CT image. (B) Bone mineral density (BMD) of trabecular (Tb) and cortical (Cort) bone as determined by  $\mu$ CT. With a sample size of 4 mice for untreated (UT) and 4 mice in Ra-223 treated group, the effect sizes (Cohen's  $d$ ) were 5.74 and 0.33 for Tb and Cort, respectively. The powers of the test for Tb and Cort were 1.00 and 0.11, respectively, using a sample

*t*-test (1-sided) and 5% significance level. Ra-223 treatment for 4 weeks caused a significant decrease in bone mineral density (BMD) of trabecular but not cortical bone. (C) Representative 3-D images of trabecular and cortical bone areas of femurs. (D) Bone parameters in Tb and Cort areas were determined by micro CT. With a sample size of 4 mice for untreated (UT) and 4 mice in Ra-223 treated group, the effect sizes were 6.32, 6.42, 5.36, 5.60 for BV/TV, BS/TV, Tb number, and Tb separation, respectively. The powers of the test for BV/TV, BS/TV, Tb number, and Tb separation were 1.00 for all four parameters, using a sample *t*-test (1-sided) and 5% significance level.



**Figure S4.** Ra-223 significantly decreased trabecular bone in female Col-GFP/B6 reporter mice 16 weeks after treatment. Eight 10-week-old female Col-GFP/B6 reporter mice were studied. Four mice were treated with one dose of Ra-223 at 300 kBq/kg, and the other four mice remained untreated (UT). Sixteen weeks later, mouse femurs were processed for  $\mu$ CT analysis. (A) Representative  $\mu$ CT image. (B) Bone mineral densities of trabecular (Tb) and cortical (Cort) bone as determined by  $\mu$ CT. With a sample size of 4 mice for untreated (UT) and 4 mice in Ra-223 treated group, the effect sizes

(Cohen's *d*) were 3.59 and 0.09 for Tb and Cort, respectively. The powers of the test for Tb and Cort were 0.99 and 0.06, respectively, using a sample *t*-test (1-sided) and 5% significance level. Ra-223 treatment for 16 weeks caused a significant decrease in bone mineral density (BMD) of trabecular but not cortical bone. (C) Representative 3-D images of trabecular and cortical bone areas of femurs. (D) Bone parameters in Tb and Cort areas were determined by micro CT. With a sample size of 4 mice for untreated (UT) and 4 mice in Ra-223 treated group, the effect sizes were 5.96, 6.46, 7.20, 10.25 for BV/TV, BS/TV, Tb number, and Tb separation, respectively. The powers of the test for BV/TV, BS/TV, Tb number, and Tb separation were 1.00 for all four parameters, using a sample *t*-test (1-sided) and 5% significance level.