















Supplemental Figure 1. 3D μCT reconstructed images of maxillae. (A-C) Healthy site in veh, OPG-Fc and ZA. (D-E) Diseased site after 11 weeks of treatment. (G-I) Diseased site after 6 weeks drug discontinuation. (J-L) Diseased site after 10 weeks discontinuation. Blue arrows point to normal alveolar bone crest in the interproximal area between the distal root of the first molar and mesial root of the second molar. Red arrow point to periodontal bone loss and areas of osteolysis. Yellow arrows point to increased bone deposition.

Supplemental Figure 2. 3D μCT reconstructed images of mandibles. (A-C) Healthy site in veh, OPG-Fc and ZA. (D-E) Drilled site after 11 weeks of treatment. (G-I) Drilled site site after 6 weeks of drug discontinuation. (J-L) Drilled site after 10 weeks drug discontinuation. Blue arrows point to normal alveolar bone crest in the interproximal area between the distal root of the first molar and mesial root of the second molar. Red arrow point to periodontal bone loss and areas of osteolysis. Yellow arrows point to increased bone deposition.

Supplemental Figure 3. Coronal  $\mu$ CT slices of the maxillary alveolar bone at the area of the first molars. (A-C) Healthy site in veh, OPG-Fc and ZA. (D-E) Diseased site after 11 weeks of treatment. (G-I) Diseased site after 6 weeks drug discontinuation. (J-L) Diseased site after 10 weeks discontinuation. Thin arrows point to areas of osteolysis. Arrowheads point to new bone deposition. (M-O) Quantification of the distance from the CEJ to ABC. \*Statistically significant different from indicated groups, p < 0.0001. \*Statistically significant different from indicated groups, p < 0.005.

Supplemental Figure 4. Axial μCT sections of the mandibular alveolar ridge. (A-C) Healthy site in veh, OPG-Fc and ZA. (D-E) Drilled site after 11 weeks of treatment. (G-I) Drilled site after 6 weeks of drug discontinuation. (J-L) Drilled site after 10 weeks drug discontinuation. Thin arrows point to areas of osteolysis. Arrowheads point to new bone deposition. (M-O) Quantification of lingual bone thickness. Statistically significant different compared to healthy mice, p < 0.0001. Statistically significant different compared to diseased mice, p < 0.0001.

different from indicated groups, p < 0.001. \*Statistically significant different from indicated groups, p < 0.05.

Supplemental Figure 5. Quantification of BV and BV/TV in the maxillae of all mice. 11 weeks of treatment (A, B), 6 weeks (C, D) and 10 weeks (E, F) after drug discontinuation.  $^{\$}$ Statistically significant different compared to healthy mice, p < 0.0001.  $^{\$}$ Statistically significant different from indicated groups, p < 0.0001.  $^{**}$ Statistically significant different from indicated groups, p < 0.001.  $^{**}$ Statistically significant different from indicated groups, p < 0.005.

Supplemental Figure 6. Representative H&E-stained images from mandible of all groups. (A-C) Healthy site of veh, OPG-Fc and ZA animals. (D-F) Drilled site at 11 weeks at the end of antiresorptive treatment. (G-I) Drilled site 6 weeks after antiresorptive discontinuation. (J-L) Drilled site 10 weeks after antiresorptive discontinuatio. Red arrows point to marginal gingival epithelium, turquoise arrows to alveolar crest, black arrows to areas of inflammation, blue arrows to periosteal bone deposition, yellow arrows to osteonecrotic areas, and green arrows to areas of bone exposure. Original magnification, x5.

Supplemental Figure 7. Quantification of histologic findings in the mandible. (A-C) The shortest epithelial-crest distance was determined. (D-F) Osteocytic lacunae were measured and empty lacunae were expressed as percent of total. (G-I) Area of osteonecrosis was measured and expressed as % of total bone area.  $^{+}$ Statistically significant different from indicated groups, p < 0.0001.  $^{**}$ Statistically significant different from indicated groups, p < 0.005.

Supplemental Figure 8. Representative sections of mandibles stained for TRAP + cells. Original magnification, x5. (A-C) Healthy site of veh, OPG-Fc and ZA animals. (D-F) Drilled site at 11 weeks, at the end of antiresorptive treatment. (G-I) Drilled site of veh, OPG-Fc and ZA 6 weeks after antiresorptive discontinuation. (J-L) Drilled site of veh, OPG-Fc and ZA 10 weeks

after antiresorptive discontinuation. (M-O) Quantification of TRAP + cell number.  $^{+}$ Statistically significant different from indicated groups, p < 0.0001.  $^{**}$ Statistically significant different from indicated groups, p < 0.001.  $^{*}$ Statistically significant different from indicated groups, p < 0.05.