Supplemental Figure legends S1-S5:

Figure S1a: EdU incorporation assay. MOSJ-Dkk1 cells proliferate faster than MOSJ-pLenti control cells. Cumulative fluorescence signal over time is proportional to the incorporated nucleoside analog EdU. Values are means +/- SD (n=4).

Figure S1b: Immunocytochemistry for β-catenin in MOSJ-Dkk1 and MOSJ-pLenti cells. The β-catenin has been visualized with a FITC-conjugated antibody (green). Nuclei have been lightly counterstained with 4',6-diamidino-2-phenylindole, dihydrochloride (DAPI). Bar= 20 μm

Figure S2: Morphology of post-confluent monolayers. During confluency, MOSJ-pLenti control cells show classical morphological signs of apoptosis whereas MOSJ-Dkk1 cells maintain stable confluent monolayers with frequent cell divisions (asterisks). Bar = 100 μm

Figure S3a: Viability of cells that received siRNA against Dkk-1. Viability (by trypan blue exclusion) and the number of recovered of cells 3 days after transfection of Dkk-1 siRNA or scrambled siRNA. Values are means +/- SD (n=3). P values $p<0.05$ = * with Student's t-test.

Figure S3b: Viability of MOSJ cells after treatment with TNKiIII or CCT063477. The number of recovered pLenti-MOSJ cells after either 20 days of post confluence or 2 days in the presence of H_2O_2 (100μM) after treatment with TNKiIII or CCT063477. The y-axes refer to the number of cells recovered from a 4 cm^2 well. Values are means +/- SD (n=3). P values $p<0.05$ = * with ANOVA and Dunnet's post-test.

Figure S3c: Western blot assays for MKK7 and p-MKK7.

Figure S4: Box and whisker plots of the average diameter of tibial medullary canals. MOSJ-Dkk1 tibias are more hollow than MOSJ-pLenti counterparts, suggesting extensive remodelling. Results displayed as box and whisker plots with the boxes representing the 25-75th percentiles, the center line representing the median, and the whiskers representing the full range of data. (n=4); *** $P< 0.001$

Figure S5: Histology of lesions in femurs Serial sections of MOS-J tumors were stained with hematoxylin and eosin **(a,e)** and trichrome **(b-d,f-h).** MOSJ-pLenti cells form tumors that displace compartments of the surrounding muscle **(a)**. Areas of cartilage, bone and fat differentiation consistent with the underlying osteochondrosarcoma phenotype are evident **(b-d).** In contrast, MOSJ-Dkk1 tumors demonstrate aggressive growth behavior **(e,f)**, with destructive soft tissue invasion and lytic bone involvement **(arrows, g)**. Note the lack of differentiation resulting in highly homogeneous masses of more primitive spindle-like cells (**h**). Bars: 1 mm.