Phosphorylated ERK1/2 expression in human primary chondrocytes expressing FGFR3<sup>WT</sup> or the heterozygous mutation G380R (ACH). (C) Immunohistology for phosphorylated ERK1/2 in femur distal growth plate of protocol 1 mice (scale bar = 100 µm). Images shown are representative of n = 9 animals per group. (D) Immunohistology for SOX9 in femur distal growth plate of protocol 1 mice (scale bar = 100 µm). Images shown are representative of n = 6 animals per group. All immunohistological data concern animals treated with protocol 1 (16 days old). Western blots are representative of 3 independent experiments.

Supplemental Figure 1. NVP-BGJ398 daily injections rescue long bone defect of Fgfr3<sup>Y367C/+</sup> mice. (A) Femur and tibia bone length measured with µCT images (Fgfr3<sup>+/+</sup> n = 8, untreated Fgfr3<sup>Y367C/+</sup> n = 9, treated Fgfr3<sup>Y367C/+</sup> n = 6, *P < 0.05 by One-way ANOVA test). Data are expressed as mean ± s.d. (B) Safranin-O staining and immunohistochemistry for Col X on histological section of tibia (scale bar = 200 µm). Asterisks show secondary ossification centers. Images shown are representative of n = 5 animals per group. (C) Immunohistochemistry for CD34 on histological section of distal tibia (scale bar = 200 µm).
Images shown are representative of n = 5 animals per group. All data concern animals treated with protocol 1 (16 days old).

Supplemental Figure 2. NVP-BGJ398 improves axial skeleton of Fgfr3<sup>Y367C/+</sup> mice. (A) X-rays of lumbar vertebrae (L4-L6), the black arrows show the L4-L6 segment and red arrow show L5 pedicle landmarks (scale bar = 2 mm). (B) Immunohistochemistry for FGFR3, Col I and Col II on lumbar IVD outlying IAF (dashed arrows) and OAF (full arrows) (scale bar = 100 µm). Images shown are representative of n = 6 animals per group. All data concern animals treated with protocol 1 (16 days old).
Supplemental Figure 3. NVP-BGJ398 improves cartilage end plate of Fgfr3<sup>Y367C/+</sup> mice. (A) Vertebra Cartilage End Plate (CEP) length (Fgfr3<sup>+/+</sup> n = 9, untreated Fgfr3<sup>Y367C/+</sup> n = 6, treated Fgfr3<sup>Y367C/+</sup> n = 6, *P < 0.05 by One-way ANOVA test). (B) Safranin-O staining and immunohistochemistry for Col X on histological section of CEP (scale bar = 200 µm). Images shown are representative of n = 6 animals per group. All data concern animals treated with protocol 1 (16 days old). Data are expressed as mean ± s.d.
Supplemental Figure 4. FGFR3 and FGFR1 expression in femoral growth plate. (A) Immunohistological analyses of FGFR3 show that the FGFR3 expression is increased in Fgfr3\textsuperscript{Y367C/+} mice and decreased after NVP-BGJ398 treatment. (B) The expression of FGFR1 revealed by immunohistochemistry is not modified in all conditions. All data concern animals treated with protocol 1 (16 days old) (scale bar = 50 \( \mu \)m). All images shown are representative of \( n = 6 \) animals per group. All data concern animals treated with protocol 1 (16 days old).
Supplemental Figure 5. NVP-BGJ398 inhibits the FGFR3 downstream signaling pathways. (A) Phosphorylated ERK1/2 and PLCγ expression in transfected human chondrocytes with FGFR3<sup>WT</sup>, FGFR3<sup>G380R</sup> (ACH), FGFR3<sup>Y373C</sup> (TDI) constructs are reduced with NVP-BGJ398. (B) Phosphorylated ERK1/2 expression in transfected HEK293-Vnr cells with FGFR3<sup>WT</sup>, FGFR3<sup>Y373C</sup> (TDI), FGFR3<sup>K650M</sup> (SADDAN) constructs are reduced with NVP-BGJ398. (C) Dose response effect of NVP-BGJ398 on phosphorylated ERK1/2 in immortalized ACH (G380R/+) and TDI (S249C+/) human chondrocytes. (IP = Immunoprecipitation, IB = Immunoblotting). (D) Immunohistological analyses of phosphorylated STAT1 show an increase expression in Fgrf3<sup>Y367C+/</sup> mice and decreased expression after NVP-BGJ398 treatment. Images shown are representative of n = 4 animals per group (scale bar = 50 µm). All data concern animals treated with protocol 1 (16 days old). Western blots are representative of 3 independent experiments.
Supplemental Figure 6. NVP-BGJ398 improves growth of the axial and appendicular skeleton in \( Fgfr3^{Y367C/+} \) mice (protocol 2)

(A) Radiographs of \( Fgfr3^{+/+} \), treated and untreated \( Fgfr3^{Y367C/+} \) skeletons show the benefit effect of the treatment (scale bar = 1 cm). (B) NVP-BGJ398 improvement of the lengths of femur, tibia, humerus, ulna, tail, radius and L4-L6 (\( Fgfr3^{+/+} \) n = 6, untreated \( Fgfr3^{Y367C/+} \) n = 5, treated \( Fgfr3^{Y367C/+} \) n = 7, *P < 0.05 by One-way ANOVA test). Data are expressed as mean ± s.d.