

Fig. S8: Quality of the cryo-EM density map of setmelanotide in the setmelanotide–MC4R–Gs–Nb35 complex. Three different views (top to bottom) on the setmelanotide ligand (purple color) and the binding calcium ion (lemon green color). All figures show the cryo-EM densities of the ligand (light blue colored mesh/volume) contoured at three different contour levels (1.5 (left), 1.0 (middle) and 0.5  $\sigma$  (right)). Setmelanotide is depicted as sticks and the calcium ion as sphere representation.