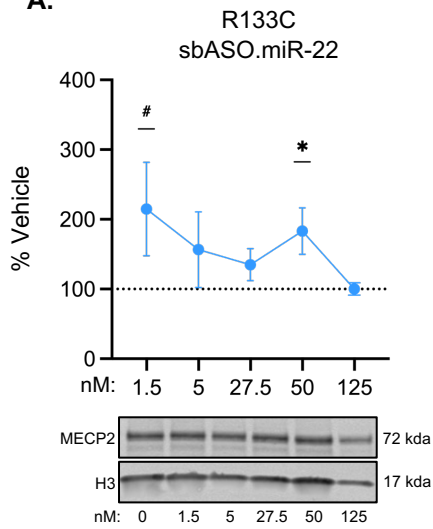
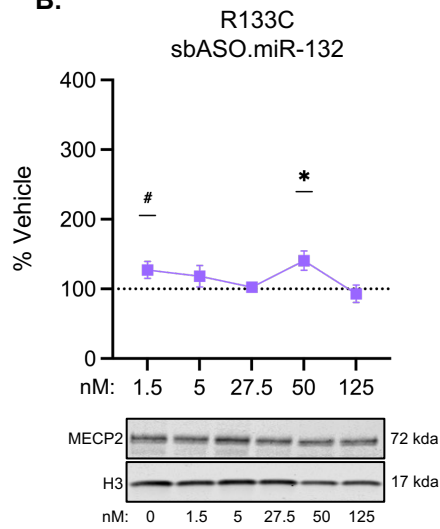
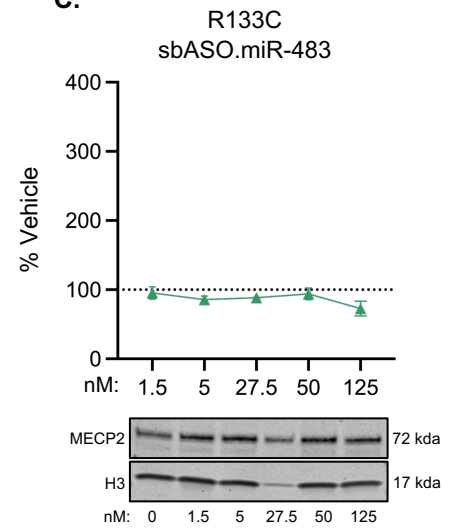
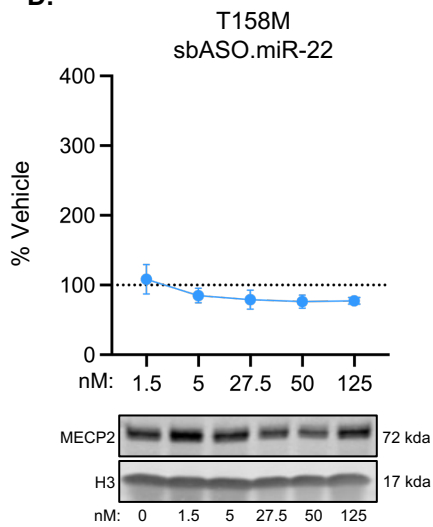
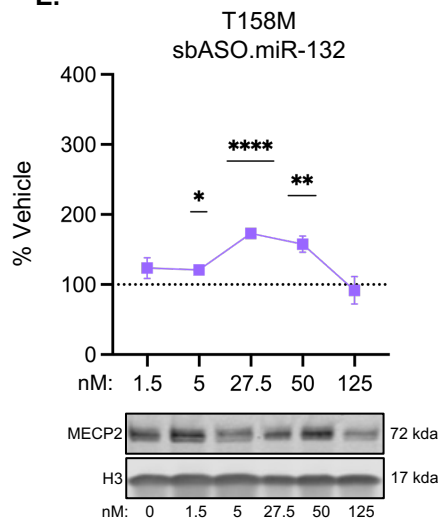
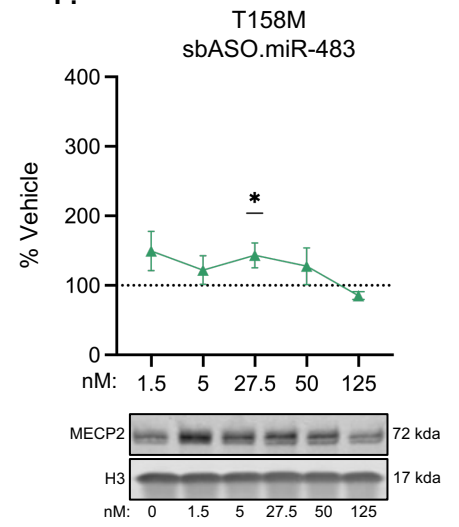
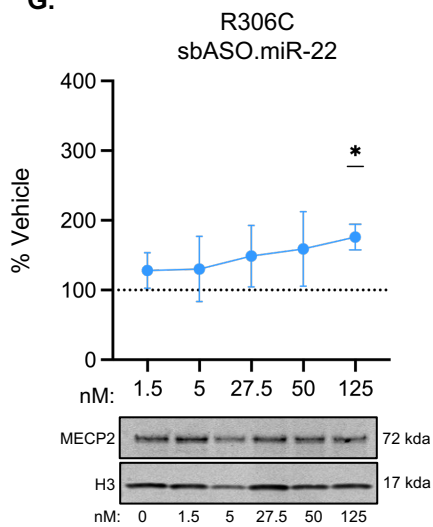
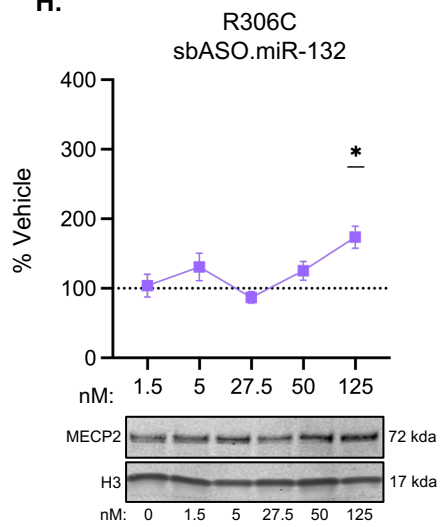
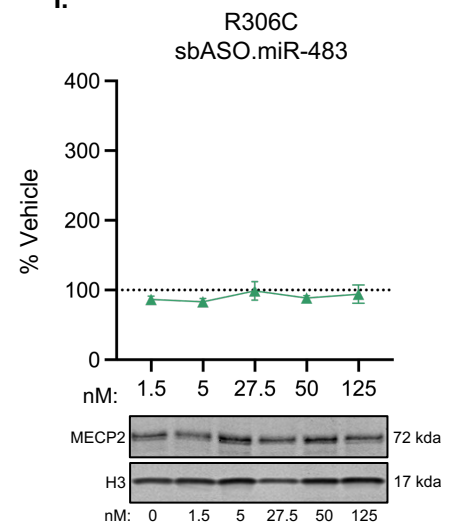


A.**B.****C.****D.****E.****F.****G.****H.****I.**

Supplemental Figure 4. Dose-Dependent Activity of sbASOs in Human-Derived Fibroblasts with Rett Syndrome Missense Mutations. Western blot analysis of the dose-dependent activity of sbASOs on MECP2 protein levels in the nuclear fraction of human fibroblast cells derived from Rett syndrome patients with missense mutations R133C, T158M, and R306C. Quantification was normalized to Histone H3 (H3) levels, with data represented as the mean percentage relative to the vehicle-treated control. sbASOs showed dose-dependent effects, increasing MECP2 protein levels across the mutations tested. Representative Western blots illustrate MECP2 levels for each treatment condition, with the MECP2 band (71 kDa) and H3 band (17 kDa) shown below the corresponding bar graphs. Outliers were identified and removed using Grubb's test at $\alpha = 0.1$. Data are presented as mean $\pm$ SEM.

sbASO.miR-22: **(A)** 1.5nM [t (df,6) = 2.344, p = 0.0575], 5nM [t (df,7) = 1.183, p = 0.2752], 27.5nM [t (df,7) = 1.744, p = 0.1247], 50nM [t (df,7) = 2.847, *p = 0.0248], and 125nM [t (df,4) = 0.05164, p = 0.9605].

(D) T158M: 1.5nM [t (df,8) = 0.3879, p = 0.7082], 5nM [t (df,8) = 1.456, p = 0.1836], 27.5nM [t (df,8) = 1.552, p = 0.1593], 50nM [t (df,8) = 2.551, *p = 0.0341], and 125nM [t (df,8) = 4.744, **p = 0.0015].

(G) R306C: 1.5nM [t (df,7) = 1.254, p = 0.2501], 5nM [t (df,7) = 0.7346, p = 0.4865], 27.5nM [t (df,7) = 1.259, p = 0.2485], 50nM [t (df,7) = 1.255, p = 0.2497], and 125nM [t (df,7) = 4.719, **p = 0.0022],

sbASO.miR-132: **(B)** R133C: 1.5nM [t (df,8) = 2.242, p = 0.0552], 5nM [t (df,8) = 1.174, p = 0.2742], 27.5nM [t (df,7) = 0.5800, p = 0.5801], 50nM [t (df,8) = 2.935, *p = 0.0189], and 125nM [t (df,7) = 0.6371, p = 0.5443].

(E) T158M: 1.5nM [t (df,8) = 1.579, p = 0.1531], 5nM [t (df,8) = 3.305, p = 0.0131], 27.5nM [t (df,7) = 18.98, ****p < 0.0001], 50nM [t (df,8) = 4.971, **p = 0.0011], and 125nM [t (df,8) = 0.4291, **p = 0.6792].

(H) R306C: 1.5nM [t (df,7) = 0.2800, p = 0.7876], 5nM [t (df,7) = 1.784, p = 0.1176], 27.5nM [t (df,7) = 1.763, p = 0.1213], 50nM [t (df,7) = 2.141, p = 0.0695], and 125nM [t (df,7) = 5.309, **p = 0.0011].

sbASO.miR-483: **(C)** R133C: 1.5nM [t (df,8) = 0.5193, p = 0.6176], 5nM [t (df,8) = 2.843, *p = 0.0217], 27.5nM [t (df,6) = 23.96, ****p < 0.0001], 50nM [t (df,8) = 0.7121, p = 0.4967], and 125nM [t (df,7) = 2.953, *p = 0.0213].

(F) T158M: 1.5nM [t (df,8) = 1.752, p = 0.1179], 5nM [t (df,8) = 1.057, p = 0.3215], 27.5nM [t (df,8) = 2.393, *p = 0.0437], 50nM [t (df,8) = 1.043, p = 0.3273], and 125nM [t (df,8) = 3.043, *p = 0.0188].

(I) R306C: 1.5nM [t (df,8) = 2.857, *p = 0.0212], 5nM [t (df,7) = 4.139, **p = 0.0044], 27.5nM [t (df,8) = 0.0901, p = 0.9304], 50nM [t (df,7) = 3.875, **p = 0.0061], and 125nM [t (df,8) = 0.4450, p = 0.6681].