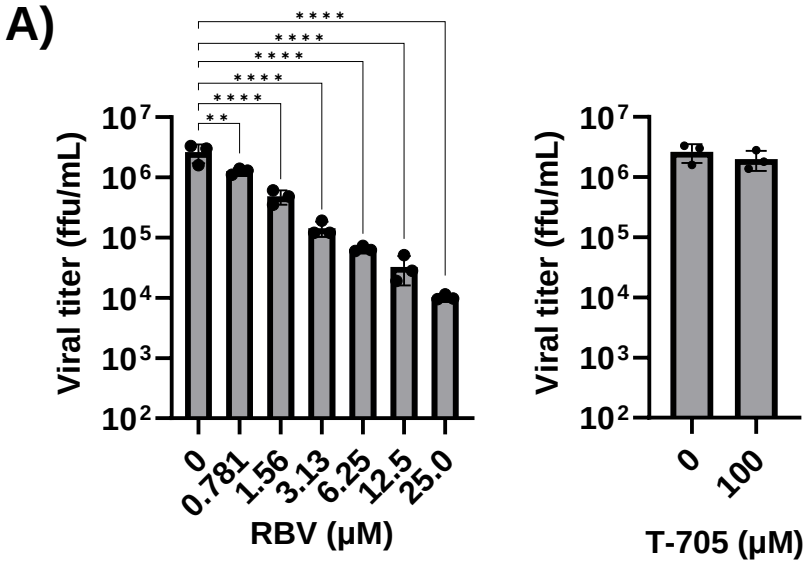

Fig. S1. *In vitro* efficacy of RBV and T-705 in NA mouse neuroblastoma cells

(A) NA cells were inoculated with RABV-CVS at a MOI of 0.01 for 1 h and cultured with medium containing RBV (left) or T-705 (right). Viral titers in supernatants were determined by the focus-forming assay. Experiments were performed in triplicate, and the data are representative of two independent experiments. Data are presented as the mean ± SD. Statistical analysis was performed by one-way ANOVA with Dunnett's *post hoc* test for RBV treatment or Student's *t*-test for T-705 treatment to compare with non-treated cells. $^{**}p < 0.01$, $^{****}p < 0.0001$.

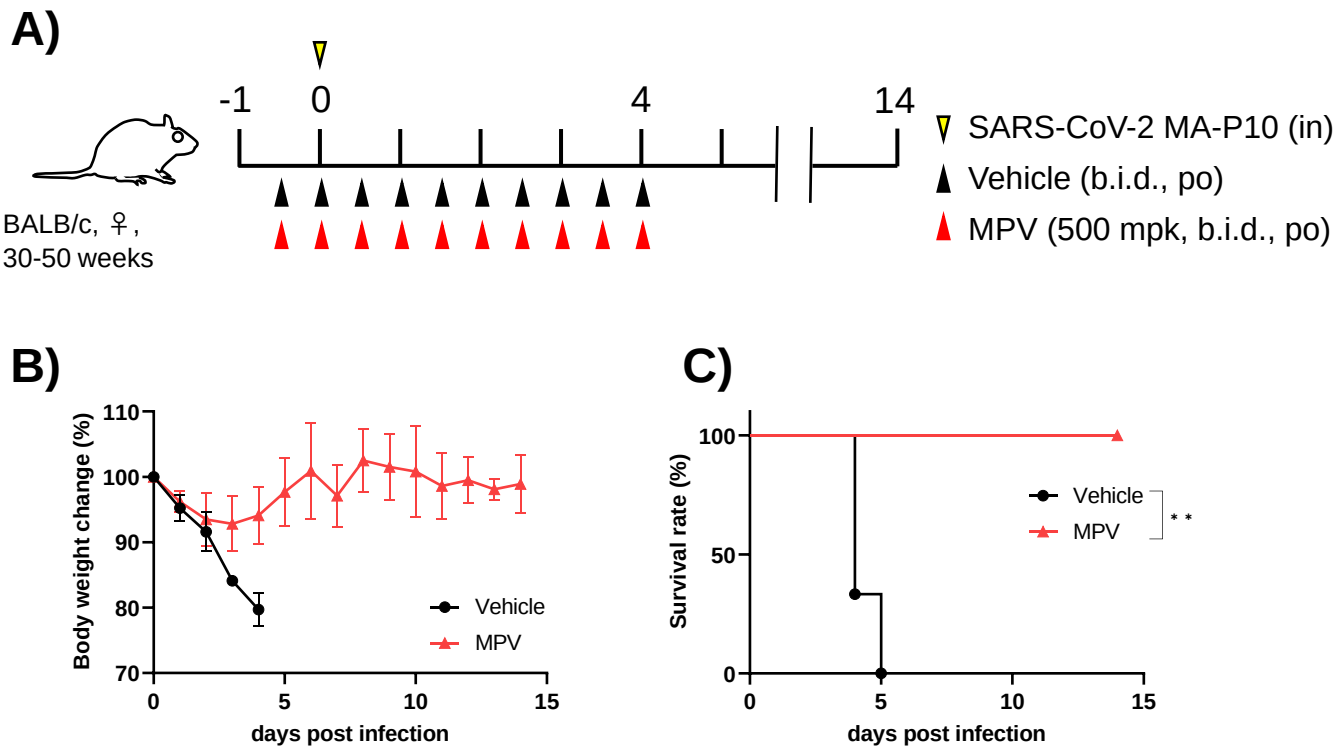

Fig. S2. *In vivo* efficacy of MPV in SARS-CoV-2–infected mice

(A) Schematic representation of the experimental design of the prophylactic administration model. Administration of vehicle or MPV to mice commenced at 1 day prior to infection (q.d., 500 mg/kg/day). On the day of infection, these compounds were administered 4 h before infection and daily thereafter until 4 dpi (b.i.d., 1,000 mg/kg/day). Mice was infected intranasally with SARS-CoV-2 MA-P10 (2.3×10^2 $TCID_{50}$/head). Infected mice were observed daily until 14 dpi; in, intranasally. mpk, milligram per kilogram. po, oral administration. **(B, C)** Body weight changes (B) and survival rates (C) of SARS-CoV-2–infected mice treated with vehicle (n = 3) or MPV (n = 5). Statistical analysis was performed by the log-rank (Mantel–Cox) test for (C). $^{**}p < 0.01$.

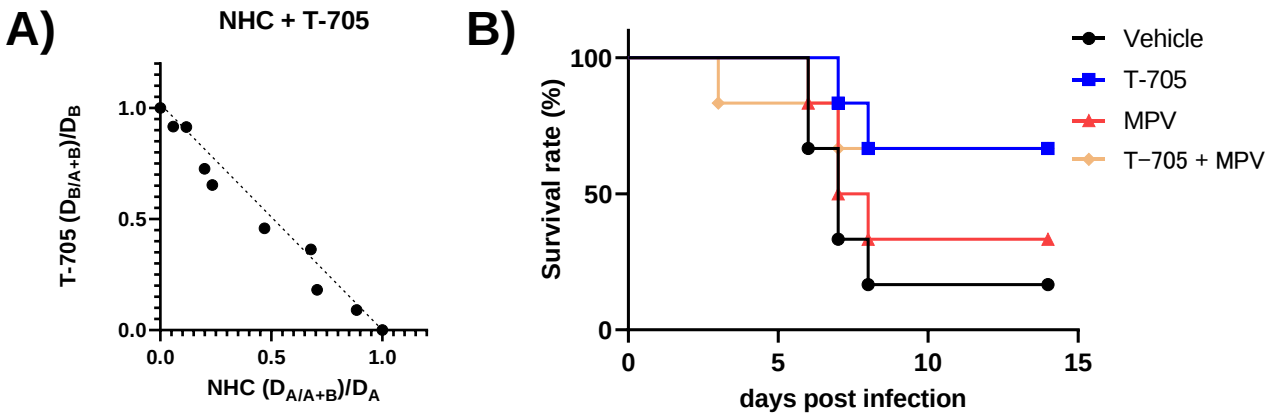

Fig. S3. The *in vitro* and *in vivo* efficacy of NHC or MPV in combination with T-705

(A) The isobologram plot of NHC in combination with T-705. D_A is the EC_{50} of NHC, D_B is the EC_{50} of T-705, $D_{A/A+B}$ is the concentration of NHC producing 50% inhibition in combination with T-705, and $D_{B/A+B}$ is the concentration of T-705 producing 50% inhibition in combination with NHC. $(D_{A/A+B})/D_A$ was plotted on the x-axis and $(D_{B/A+B})/D_B$ was plotted on the y-axis. The dashed line represents the reference line of the additive effect. The data are representative of two independent experiments. **(B)** Survival rates of RABV-CVS–infected mice treated with vehicle (n = 6), MPV alone (n = 6), T-705 alone (n = 6) or T-705 and MPV combination therapy (n = 6). Mice were orally administered vehicle, MPV (500 mg/kg), T-705 (500 mg/kg) or mixture of T-705 (500 mg/kg) and MPV (500 mg/kg) from 1 day prior to RABV infection (q.d.). Mice were infected intramuscularly with RABV-CVS (5×10^5 FFU/head). After viral infection, each compound was orally administered daily until 7 dpi (b.i.d.). Statistical analysis was performed by the log-rank (Mantel–Cox) test. No significant difference was observed in survival between T-705 alone and T-705/MPV combination.