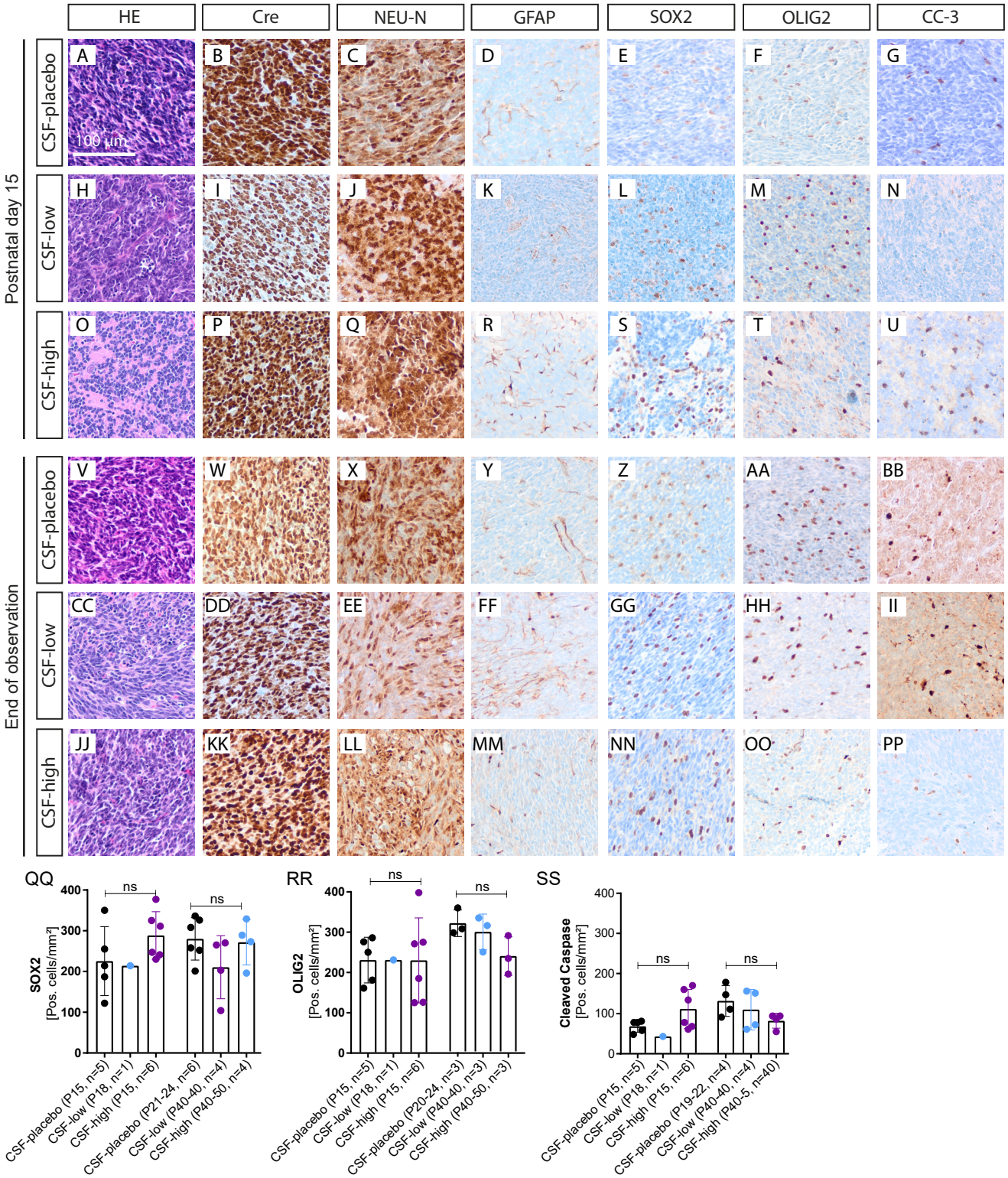
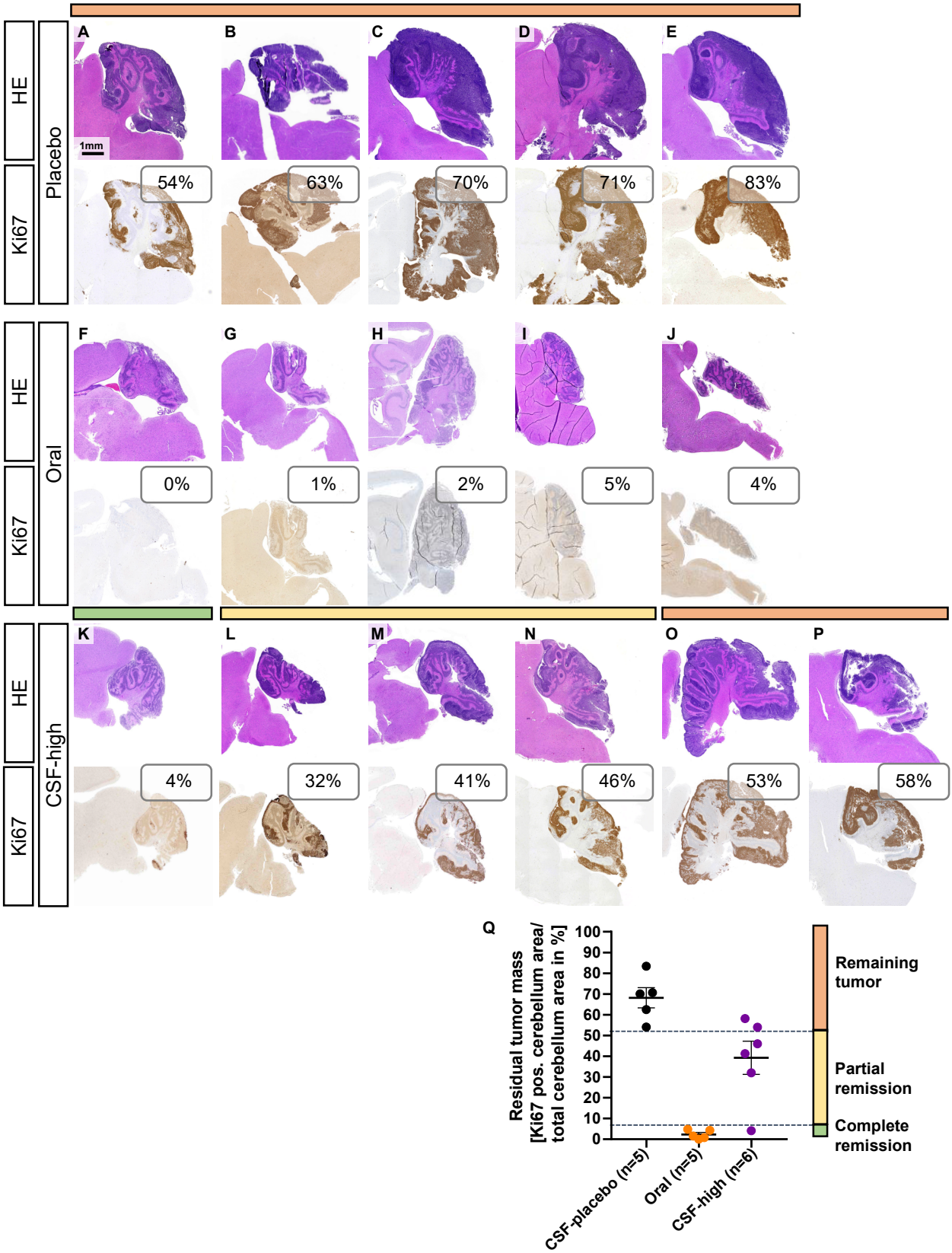
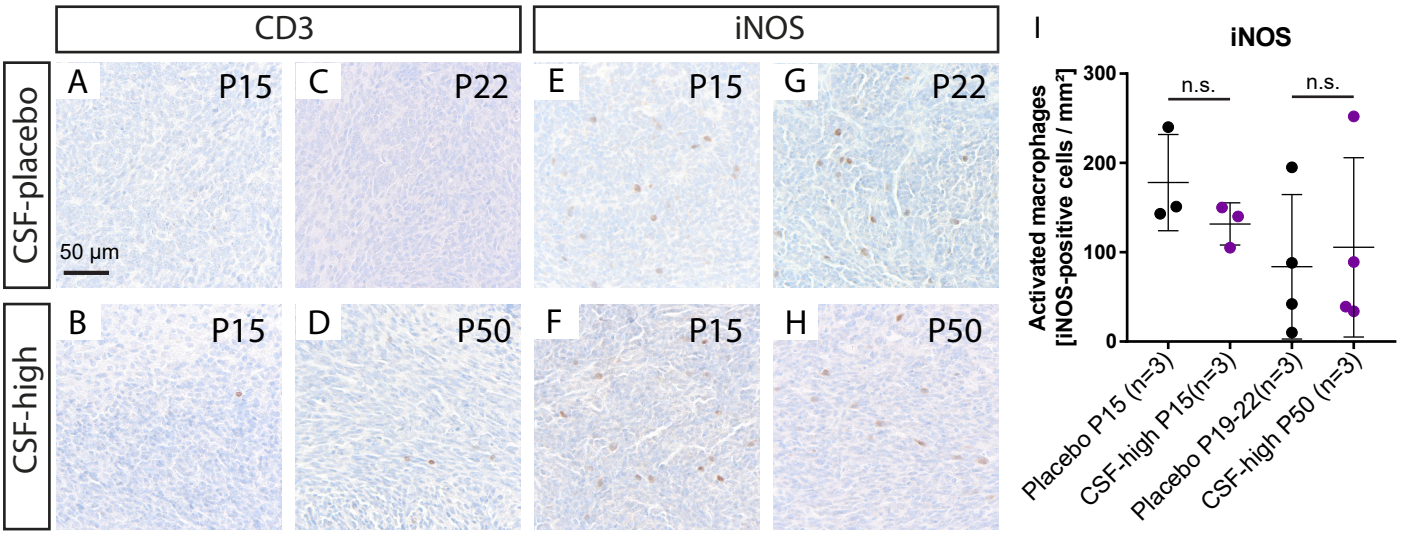


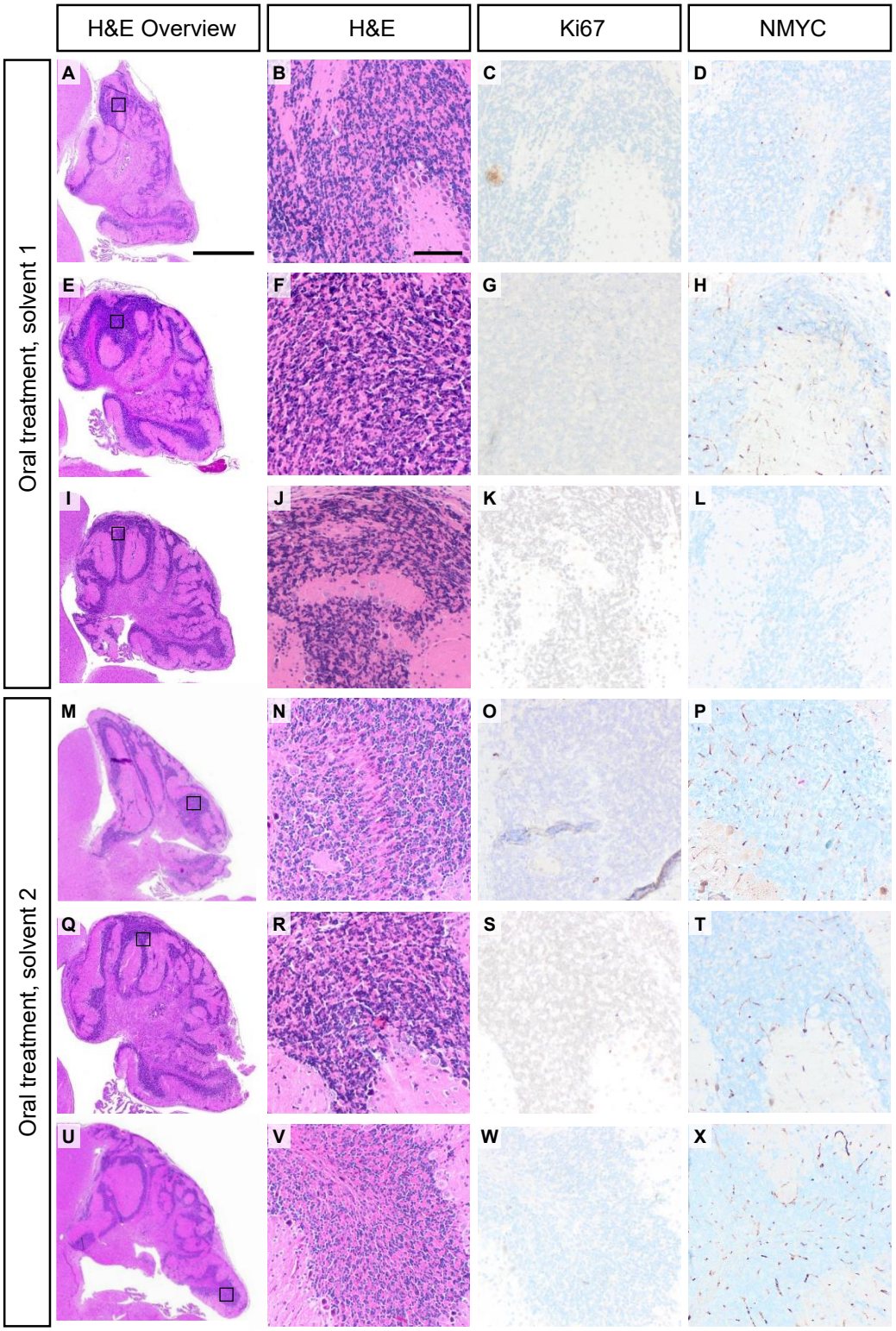
Supplementary Figure 1: Immunohistochemical stainings of neuronal and glial differentiation markers and an apoptosis marker in tumors at P15 and P50. No relevant differences in the expression of NeuN, GFAP, OLIG2, SOX2, and Cleaved Caspase-3 was detected between the treatment groups CSF-placebo, CSF-low, and CSF-high. Tukey's test was performed, p values >0.05 were rated not significant.



Supplementary Figure 2: Response evaluation on day 15 shows a promising effect of intraventricular treatment with Vismodegib. Median sagittal H&E and Ki67 stained brain sections of all observed treatment groups on day 15 are shown **(A-P)**. The treatment response was evaluated by the relative proliferative cerebellar area (Ki67 positive cerebellum area/ total cerebellum area in %) and is shown in the upper right corner of each Ki67 stained brain section. Placebo treated mice display a residual tumor mass of 54-83% **(A-E)**. The residual tumor mass of orally treated mice is 0-5% **(F-J)**. Based on these results, three outcomes were defined: Complete remission with a tumor mass of ≤ 5%, residual tumor with a tumor mass of ≥ 50%,and partial remission with a tumor mass of 6-49% **(U)**. Within the CSF-high group one tumor is in complete remission **(K)**, three are in partial remission **(L, M, N),**and two have remaining tumors **(O, P)**. Scale bar in Panel A corresponds to 1mm in all panels.



Supplementary Figure 3: Immune microenvironment in Placebo treated and CSF-high treated *Math1-cre::Ptch1Fl/Fl* mice. Immunostaining for CD3 reveals little to no immune infiltration by T-cells both after Placebo and CSF-high treatment at an early time point after treatment (P15) (A-B) and at sacrifice due to tumor-related symptoms (P19-P22 for placebo, P47-P50 for CSF-high) (C-D). Immunostaining for iNOS reveales comparable numbers of M1 activated macrophage per tumor area after placebo and CSF-high treatment at both time points (E-H). Qantification of iNOS-positive cells in 4 non-overlapping high power fields per tumor shows no significant difference between placebo and CSF-high treatment (student's t-test, $p>0.05$ in both comparisons).



Suppl. Fig. 4: Cell accumulation found in orally treated group consists of non-tumor cells. H&E stained sagittal sections of the cerebella of orally treated mice show cell accumulations at the end of observation (**A, E, I, M, Q, U**). Squares mark the corresponding high power fields. The cells are monomorphic, tightly packed, small, and hyperchromatic (**B, F, J, N, R, V**). No considerable proliferation was observed within the cell accumulations (**C, G, K, O, S, W**). Furthermore, no NMYC signal was detected (**D, H, L, P, T, X**). Scale bars correspond to 1000 µm in panels **A, E, I, M, Q** and **U** and to 50 µm in panels **B-D, F-H, J-L, N-P, R-T** and **V-X**.