**Supplementary figure 1.** Consensus NMF of 81 primary ependymoma samples at k = 3 delineates two posterior fossa subgroups in the study cohort.

**Supplementary figure 2.** STAT3, IL6 and inflammatory response pathway signaling associated gene expression is upregulated in Group A EPN.GSEA enrichment plots of (**A**) STAT3 transcriptional factor target motif genes, (**B**) experimentally validated STAT3 target genes, (**C**) BioCarta IL6 pathway genes and (**D**) BioCarta inflammatory response genes. NES, normalized enrichment score; FDR, false discovery rate.

**Supplementary figure 3.** Ratio of Group A EPN IL6/STAT3 pathway genes in tumor versus the myeloid compartments. Error bars represent SEM.

**Supplementary figure 4. Concentration of cytokine secretion from flow-sorted disaggregated tumor samples**. Cells were cultured for 96hours in O15 and normalized to 106 cells. Supernatants were run on a high sensitivity Milliplex cytokine array. P-values were calculated using 1-tailed t-tests.

**Supplementary figure 5. S3I-201 effects on cell cycle of EPN cell line 811 and apoptosis in EPN cell line 723.** (**A-B**) Inhibition of cell proliferation by STAT3 inhibitor S3I-201 was assessed by MTS and 3H-thymidine incorporation in 811 and U87 cells. By both assays, 811 cells were more sensitive than constitutively STAT3-activated U87 cells. Graphs are representative experiments. (**C**) Cell cycle analysis of EPN cell line 811 with treatment of 150uM S3I-201 for 24hours. Experiments were run in triplicate. (**D**) Real-time quantification of cleaved Caspase 3/7, representative of apoptosis, over 72 hours of S3I-201 treatment. Graph combined 3 experiments with 6 replicates per experiment and shows accumulation of cleaved caspase 3/7 normalized to cell numbers. P-value calculated using 2-tailed t-test (**E**) Western blot validation of STAT3 inhibition by S3I-201 after 24hours of treatment, as measured by decreased STAT3 phosphorylation and reduced STAT3-regulated factors. (**F**) IL6 secretion from 811 cells treated with S3I-201 for 24hours in 2ml O15. p-values were calculated using 2-tailed t-test.

**Supplementary figure 6. IL6 is the driving cytokine for immune suppressive phenotype observed in 811 CM monocytes.** (**A**) Cytokine secretion from 811-conditioned media (811CM) used in CD14+ monocyte experiments. (**B**) IL8 secretion from flow-sorted CD14+ PBMCs incubated in 811 CM, 811 CM+100µg/ml cetuximab (811CM+Cetux) or 811 CM + 100µg/ml trastuzumab (811CM+Tras) for 96 hours. (**C**) Median Fluorescent Intensity (MFI) of pSTAT3 from CD14+ monocytes incubated with the various media.