Brain tumours account for just 2% of cancer, but are the most common cause of cancer-related death in children. Currently treatment consists of surgery followed by adjuvant chemotherapy and/or radiotherapy. Survival rates have generally increased, but many survivors suffer from radiotherapy related neurocognitive and endocrine side effects as well as an increased risk of secondary cancer. Adjuvant chemotherapy is normally multimodal to circumvent chemoresistance, but several studies have demonstrated it be ineffective in the absence of radiotherapy. The identification of children with drug resistant disease at the outset could allow stratification of those that are potentially curable by chemotherapy alone. Ultimately, however, what is required is a means to overcome this drug resistance and restore the effectiveness of chemotherapy. We have investigated two different types of children’s brain tumours: medulloblastomas, which are frequently described as chemoincurable, and ependymomas, which are often chemoresistant and highly prone to local relapse. Since the majority of chemotherapy drugs used are substrates for ABCB1 we hypothesised that ABCB1 may be underlying this drug resistance. In each tumour type we have identified a sub-population of ABCB1 expressing cancer stem cells. ABCB1 positivity correlates with relapse and poor overall survival of ependymoma patients; whilst identifying high-risk medulloblastoma patients. Using patient derived cell lines, that retain ABCB1 positive cancer stem cells, we have repurposed a drug, normally used to treat pulmonary hypertension in children, in circumvention of this resistance.