n=5, YM155 n=6). For (D-F), mice were treated with vehicle (saline) or YM155 (10 mg/kg/day) via micro-osmotic pump (vehicle n=6, YM155 n=5). Caliper measurements were made twice a week to monitor tumor growth (A,D) and resulting tumors were collected, photographed (B,E), and weighed (C,F). Experiments were repeated 2 (A-C) and 3 times (D-F) respectively. Both intra-tumoral and systemic treatment with YM155 decreased tumor size over time compared to vehicle control. ($p<0.02$ for IT and pump YM155 tumor weight by ANOVA with post hoc student's t-test). Error bars represent SEM.

Supplementary Figure 1. YM155 inhibits survivin expression in MB cells. *Ptch* mutant tumor cells were treated with DMSO (D) or YM155 (Y) for 48 hours and analyzed for expression of *survivin* by real time PCR (A) and by western blotting after 24 hr. (B) YM155 dose in (B) is 1μM. YM155 decreases Survivin expression at both the RNA and protein level. Data are representative of 3 experiments.

Supplementary Figure 2. LLP3 inhibits proliferation of *Ptch* mutant tumor cells. (A) *Ptch* mutant tumor cells were treated with DMSO or multiple doses of LLP3 for 48 hr and pulsed with 3H-thymidine for 12 hr to measure proliferation. Treatment decreased proliferation in a dose-dependent manner ($p<0.05$ by ANOVA with post hoc student's ttest). Data represent mean +/- SD and are representative of 3 experiments.

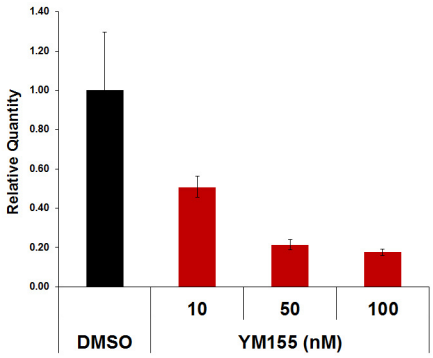
Supplementary Figure 3. Survivin antagonists kill GNPs but not do not affect survival of post-mitotic neurons. Granule Neuron Precursors (GNPs) were isolated from P7 wild type cerebella, split into two treatment groups, and plated in either SHH-containing media (A) or differentiation media (B). Cells in SHH-containing media were treated immediately with DMSO, YM155, or S12 for 48 hr and incubated with ethidium homodimer1 (EthD1) to mark dead/dying cells (A). Cells in differentiation media were cultured for 5 days, followed by treatment with DMSO, YM155, or S12 for 48 hr and incubation with EthD1 to mark dead/dying cells (B). Both S12 and YM155 caused GNP cell death at high doses ($p<0.01$

for high doses. NS for 50nM YM155 and 10µg/ml S12), but did not kill PMNs (P>0.2, NS for all doses). Data represent mean +/- SD and are representative of 4 independent experiments.

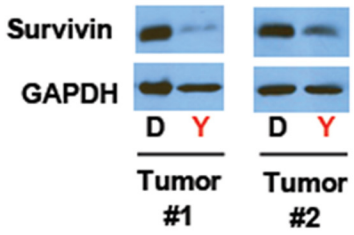
Supplementary Figure 4. Survivin is highly expressed in patient derived xenografts of MB. RNA was isolated from human fetal cerebellum (hFC), adult cerebellum (hAC), and PDX tumors DMB012, DMB018, and ICb-984MB and analyzed for Survivin expression using real time PCR. Survivin is highly expressed in PDX tumors. Expression was not detected in hAC above background (RQ < 0.05). Data are plotted relative to hFC and error bars represent 95% confidence interval calculated using sum of the squares method.

SNB Supplementary Figure 1

A.

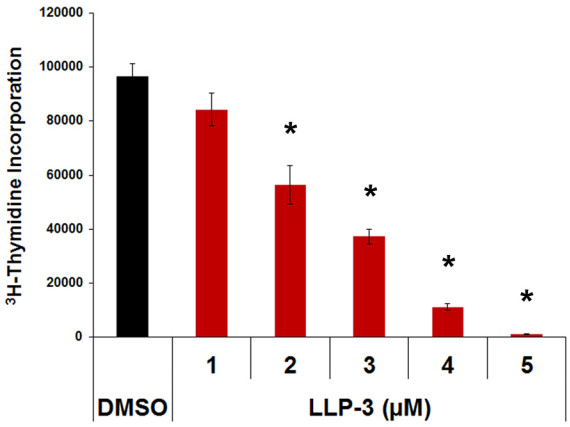


B.

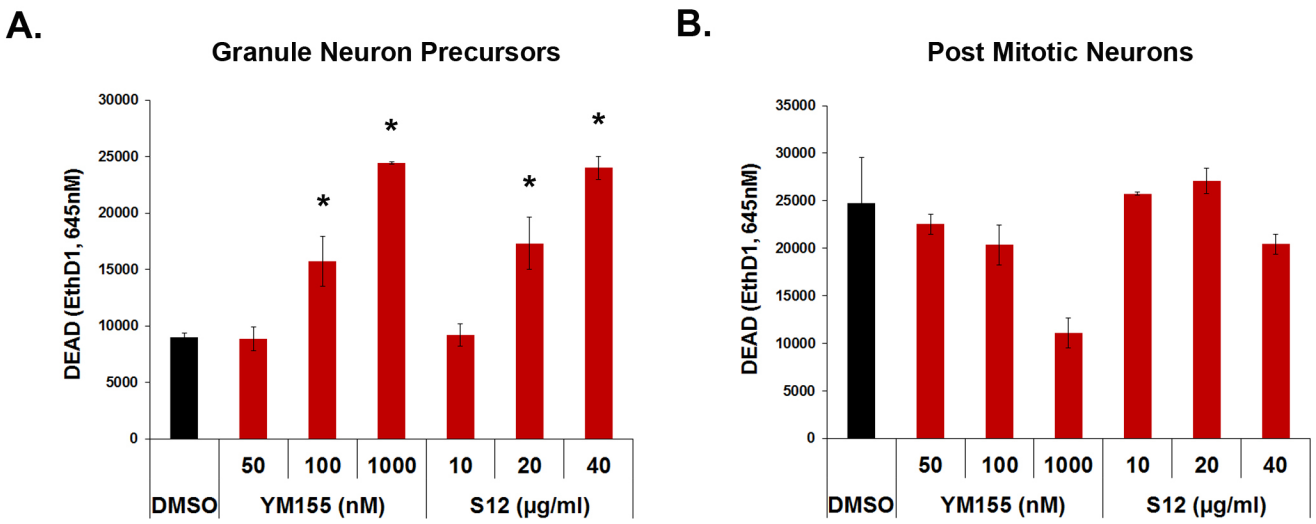


SNB Supplementary Figure 2

A.



SNB Supplementary Figure 3



SNB Supplementary Figure 4

A.