Supplemental Figure 1: Cell cycle progression occurs more rapidly in CD15+ cells than in CD15- cells. (A-E) CD15+ and CD15- cells from germline *patched* mutant tumors were pulsed with BrdU for 30 minutes, washed, and then analyzed immediately (30 min) or cultured for an additional 6, 12 or 24 hours. (A, B) Graph showing proportion of BrdU-labeled CD15- (A) and CD15+ (B) cells within each phase of the cell cycle (based on flow cytometric analysis of BrdU and DNA content) at the indicated time points. Numbers indicate percent of cells in each cell cycle phase. Note that the proportion of BrdU-labeled cells in S phase decreases more rapidly in the CD15+ population compared to the CD15- population, while the proportion of cells in G1 phase increases more rapidly in the CD15+ population, suggesting that CD15+ cells move out of S phase and progress through the cell cycle faster than CD15- cells. (C-E) Percentage of BrdU-labeled cells in early (C), mid (D), or late (E) S phase at each time point. The percentage of cells in each component of S phase decreases more rapidly (as denoted by the steeper slope) in the CD15+ population than in the CD15- population. (F-L) CFSE analysis of cell divisions in CD15+ and CD15- populations. Cells were labeled with CFSE for 20 minutes immediately after sorting into CD15+ and CD15- populations, and then analyzed for CFSE fluorescence by flow cytometry at the indicated time points. (F-I) Histograms and median fluorescence intensity values of peaks of CFSE-labeled cells with highest ("Peak 0 median") and lowest ("Peak x median") fluorescence are shown for t=0 (F), 48 hours (G), 72 hours (H), and 96 hours (I). At each time point, the majority of the CD15+ cells have undergone more cell divisions (based on lower values for the peak with the lowest fluorescence) than CD15- cells. (J-L) Proportion of cells within each peak at 96 hours after labeling was determined using the "Proliferation" analysis function in FlowJo software. The number of peaks was defined based on the median fluorescence of the least fluorescent peak (12.2) in the CD15+ population compared to the peak with the highest fluorescence (163; representing undivided cells) in the CD15- population. Histograms represent FlowJo assignment of peak placement in CD15+ (J) and CD15- (K) populations. (L) Graph represents percentage of cells within each peak corresponding to 0, 1, 2, 3, or 4 cell divisions. By 96 hours, the majority (86%) of CD15+ cells had undergone 4 divisions, while most of the cycling CD15- cells had undergone only 1, 2, or 3 cell divisions.

Supplemental Figure 2: Aurk and Plk inhibitors block proliferation of *patched* mutant tumor cells. (A, B) Cells from conditional *patched* mutant tumors were cultured in the presence of the indicated concentrations of VX-680 (A) or BI-2356 (B), pulsed with ^{3}H-Td at 48 hours, and harvested for analysis of ^{3}H-Td incorporation at 66 hours. IC50 values were calculated using the log(inhibitor) vs. response equation (Y=Bottom + (Top-Bottom)/(1+10^((X-LogIC50))) in GraphPad Prism software. (C, D) Germline *patched* mutant tumor cells were treated with the SHH antagonist LDE-225 or the indicated Aurk inhibitors (C) or Plk inhibitors (D), and ^{3}H-Td incorporation was assessed as described above. Data represent means of triplicate samples ± SEM. Aurk inhibitors significantly reduced ^{3}H-Td incorporation ($p < 0.05$ based on paired 2-tailed t-tests), with the exceptions of PHA-739358 (100 nM), CYC116 (100 nM), PHA-680602 (100 nM), CCT129202 (500 nM and 100 nM), and ENMD-2076 (500 nM and 100 nM). All Plk inhibitors significantly reduced ^{3}H-Td incorporation ($p < 0.005$).

Supplemental Figure 3: Aurk inhibitor cooperates with SHH antagonist and chemotherapeutic agents. Conditional *patched* mutant tumor cells were treated with increasing concentrations of LDE-225 (A), Vincristine (B), Cisplatin (C), or Cyclophosphamide (D) alone or in combination with 30 nM VX-680, pulsed with ^{3}H-Td at 48 hours, and harvested for analysis of ^{3}H-Td incorporation at 66 hours. IC50 values were calculated using the log(inhibitor) vs. response equation (Y=Bottom + (Top-Bottom)/(1+10^((X-LogIC50))) in GraphPad Prism software.

Supplemental Figure 4: Plk and Aurk inhibitors enhance sensitivity to radiation. Germline *patched* mutant tumor cells were cultured in the presence of DMSO (A, B), 10 nM BI-2536 (A), or 30 nM VX-680 (B) for 24 hours, treated with increasing doses of radiation (0, 0.25, 0.5, or 1 Gy), and cultured for an additional 24 hours. The cells were pulsed with ^{3}H-Td at 48 hours and harvested for analysis of ^{3}H-Td incorporation at 66 hours. Data represent means of triplicate wells ± SEM.

Supplemental Figure 5: Aurk inhibitor blocks tumor growth *in vivo*. Mice bearing subcutaneous allografts of germline *patched* mutant tumor cells were treated twice daily with vehicle (5% Dextrose) or 30 mg/kg PHA-739358. (A) Tumor volume was measured using calipers. Arrows indicate start of treatment, and each line represents an individual mouse. (B) Images of tumors. (C) Tumor weights. Each point represents a single tumor, and grey lines represent the mean tumor weights, which were significantly different ($p < 0.01$, based on paired two-tailed t-test between the vehicle and PHA-739358 group).

Supplemental Figure 6: Classification of human MB xenografts. (A) Medulloblastoma subgroups were assigned by NanoString assay and PAM classification. Heat maps depict the expression of subgroup-specific markers for the training cohort (54) and xenograft samples. Subgroup assignments are indicated above the heat map. All tumors were classified with ≥ 99% confidence probability. (B) Principal component analysis on NanoString expression profiles of medulloblastoma samples. Background gradient depicts the confidence probabilities of the trained PAM classifier in the vector space spanned by the first two principal components of the training data. White boundaries represent decision boundaries between medulloblastoma subgroups.