

Supplementary Figure Legends

Supplementary Figure 1. PDX models of HNSCC express 5T4. Hematoxylin and eosin staining and immunohistochemistry for 5T4 (brown color) in PDX-SCC-M0, PDX-SCC-M1, and PDX-SCC-M11 models.

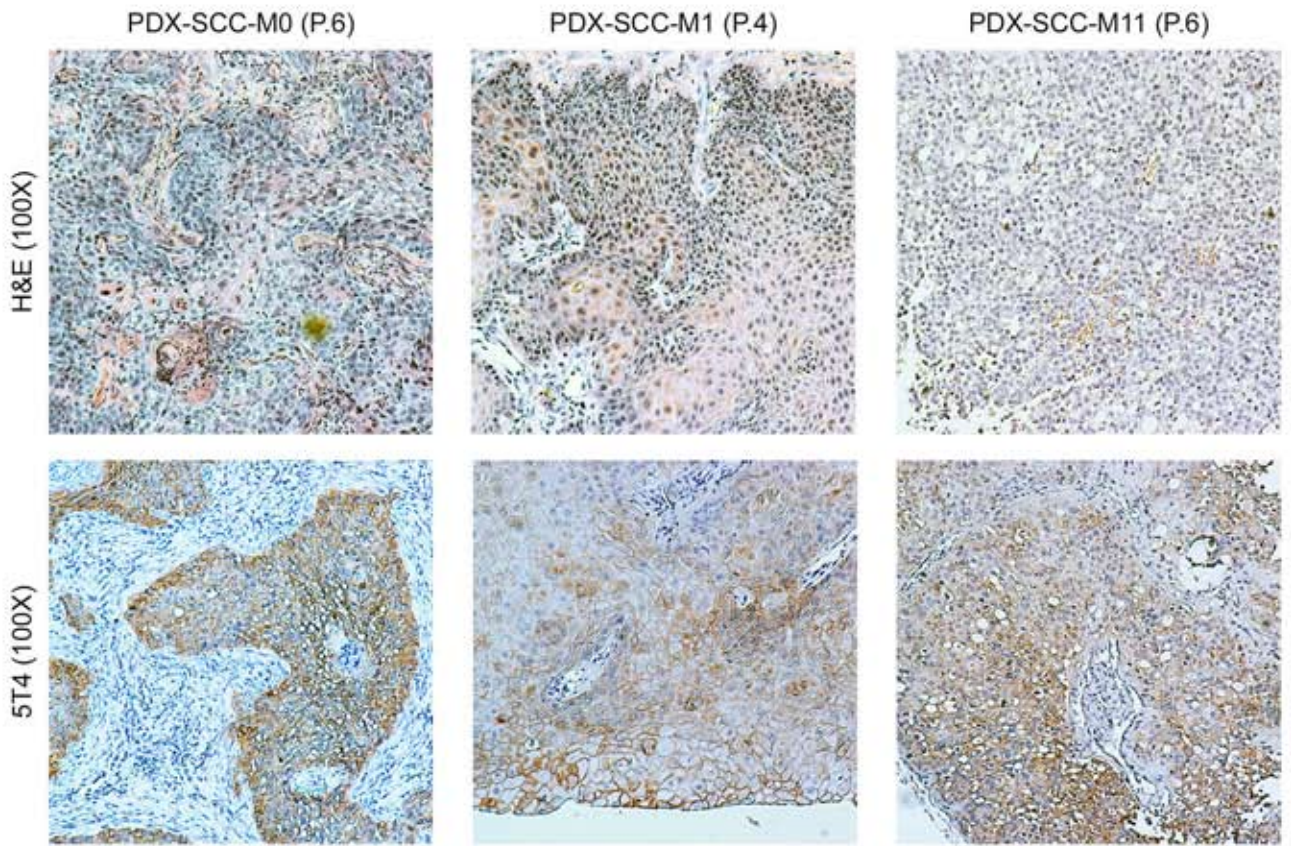
Supplementary Figure 2. 5T4 expression co-localizes with cancer stem cells (*i.e.* CD44^{high}) in HNSCC PDX tumors. Immunofluorescence of untreated PDX-SCC-M0 tumors showing 5T4 (red) and CD44 (green) expression patterns. White arrows point to 5T4^{high}CD44^{high} cells.

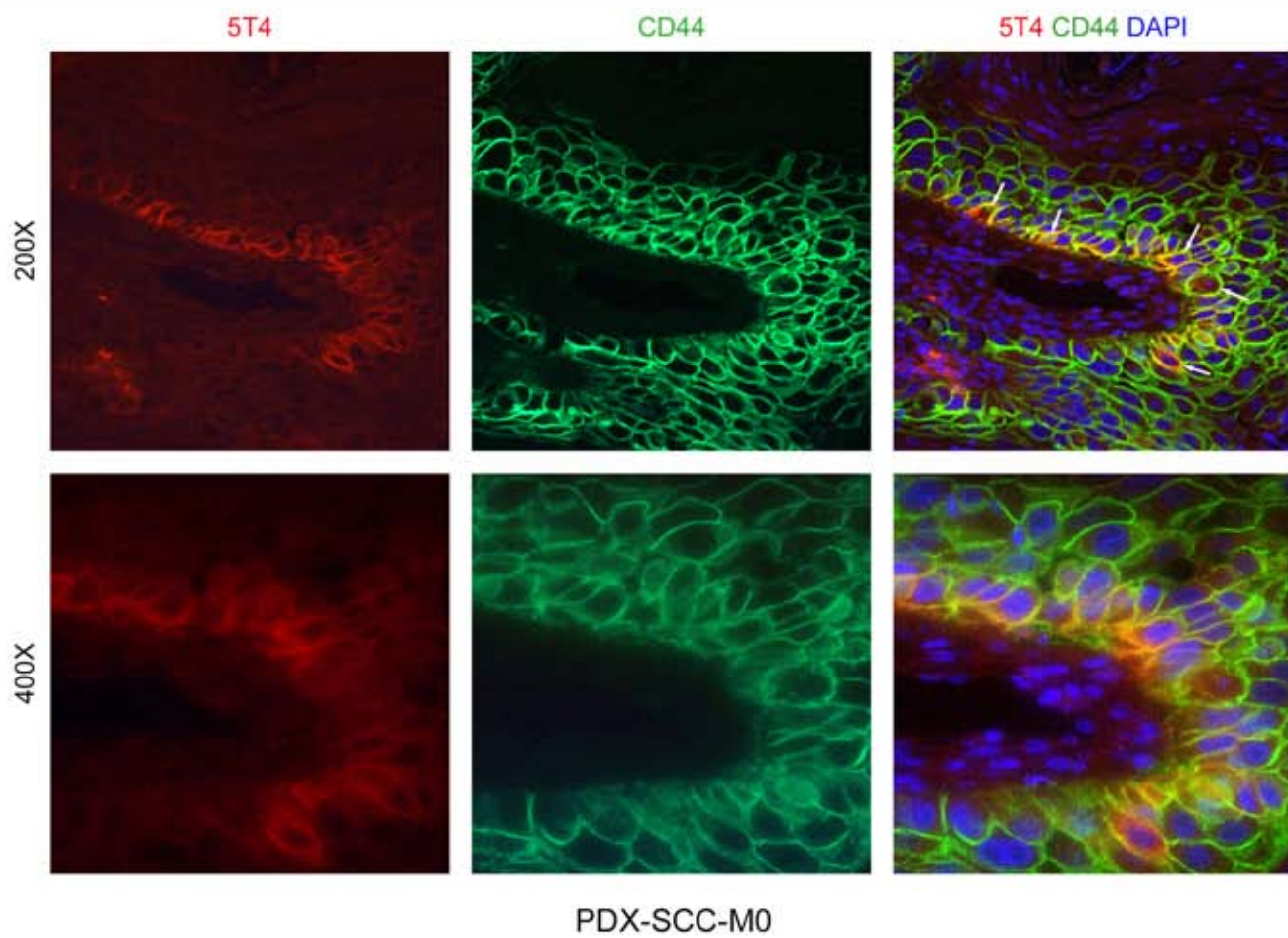
Supplementary Figure 3. Effect of MEDI0641 on HNSCC cell number in cell lines exhibiting intermediate (UM-SCC-74B) or low (UM-SCC-14B) 5T4 expression levels. Graphs showing the effect of 72-hour treatment with 0.5 or 1 µg/mL MEDI0641, as compared to 1 µg/mL IgG-PBD control, in UM-SCC-14B and UM-SCC-74B cells. Asterisks depict $p < 0.05$.

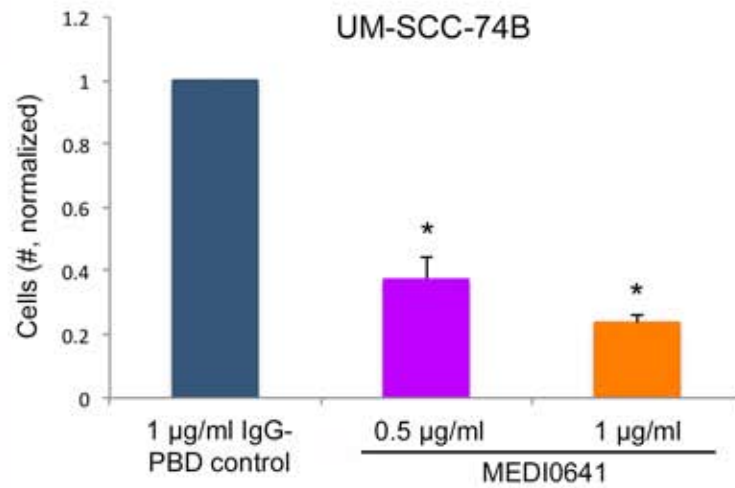
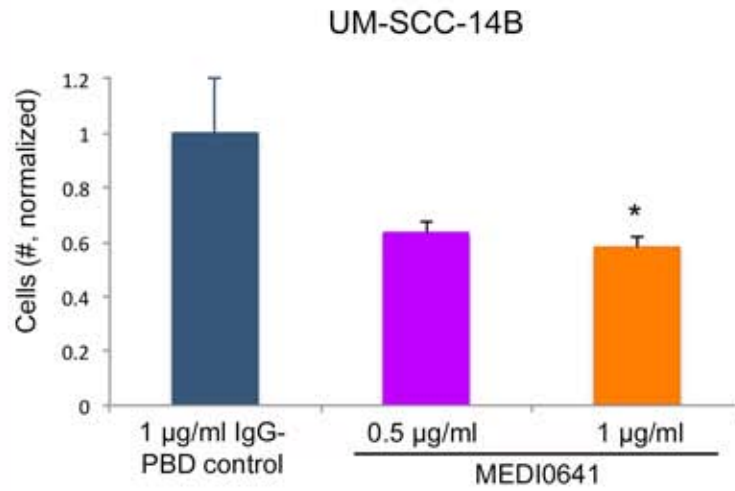
Supplementary Figure 4. MEDI0641 reduces the CSC fraction in the PDX-SCC-M11 model. **(A)** Figures showing the gating used for flow cytometry analysis of ALDH and CD44 activity in tumors treated with 1.0 mg/kg IgG1-PBD control or MEDI0641. A graph depicting the change in ALDH and CD44 activity in the IgG1-PBD control and MEDI0641 groups. **(B)** Graphs depicting the mean tumor volumes and mean mouse weights. of the IgG1-PBD control and MEDI0641 groups during the 7 day treatment period. **(C)** Actual pictures of the resected tumors from the IgG1-PBD control and MEDI0641 groups. Graphs depicting the tumor volumes and tumor weights of each tumor in the IgG1-PBD control and MEDI0641 groups.

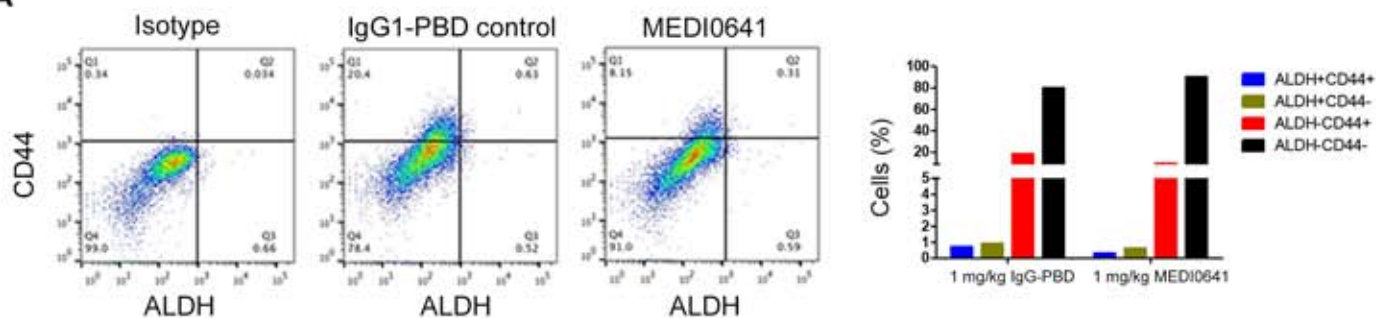
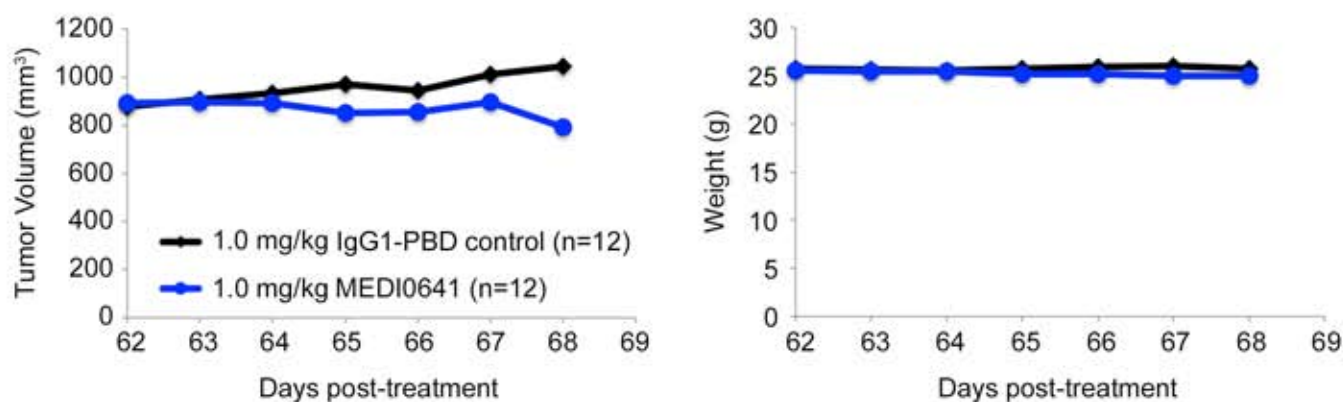
Supplementary Figure 5. MEDI0641 reduces the fraction of cancer stem cells. Graph displaying the effect of a single dose of 1 mg/kg MEDI0641 or 1 µg/mL IgG-PBD on the fraction of CD44^{high} cells (FACS) in PDX-SCC-M11 tumors (7 days after injection).

Supplementary Figure 6. MEDI0641 prevents local recurrence following surgery in the PDX-SCC-M11 model. A Kaplan-Meier curve depicting the results of a second independent recurrence experiment in mice treated with either IgG1-PBD control or MEDI0641 prior to surgical tumor removal.







A**B****C**