**Supplemental Figure 1. *Combined treatment with radiation and tumor-specific mAb or IC does not impact mouse weight.*** Treatment with hu14.18K322A and radiation in **A)** B78 melanoma-bearing C57BL/6 mice or **B)** NXS2 neuroblastoma-bearing A/J mice did not cause weight changes to suggest additional toxicity compared to animals receiving sham radiation and control IgG (*p* = 0.907, C57BL/6 mice; *p* = 0.633, AJ mice). **C)** Treatment of B78 tumors with hu14.18-IL2 and radiation does not significantly impact animal weight (*p* = 0.290) compared to control IgG.

**Supplemental Figure 2.** ***Following radiation, IT injection of hu14.18K322A improves tumor response compared to IV delivery.*** In B78 melanoma-bearing C57BL/6 mice treated with 12 Gy radiation, we observed improved tumor response with IT versus IV administration of hu14.18K322A. \* *p* = 0.02.

**Supplemental Figure 3. *SCC1-C cells are not sensitized to radiation by cetuximab in vitro and remain susceptible to cetuximab-mediated ADCC.*** **A)** *In vitro* clonogenic assays demonstrated no significant effect of cetuximab on the intrinsic sensitivity of SCC1-C cells to radiation (*p* = 0.222). **B)** Despite this lack of radiosensitization and prior demonstration of resistance of SCC1-C cells to *in vitro* proliferative inhibition with cetuximab ([19](#_ENREF_19)), 51chromium cytotoxicity assays demonstrated that non-radiated SCC1-C cells remain susceptible to cetuximab-mediated ADCC by fresh human peripheral blood mononuclear cells as effector cells. This is consistent with previously reported data showing persistent expression of EGFR in the plasma membrane of these cetuximab-resistant cells ([19](#_ENREF_19)).

**Supplemental Figure 4. *Hu14.18K322A and hu14.18-IL2 do not impact intrinsic cell sensitivity to radiation in vitro and radiation does not impact GD2 expression but GD2-expression is required for the cooperative in vivo interaction of radiation with hu14.18K322A or hu14.18-IL2.*** *In vitro* clonogenic assays demonstrate no significant effect of hu14.18K322A on the intrinsic sensitivity of **A)** B78 (*p* = 0.765) or **B)** NXS2 cells (*p* = 0.945) to radiation. For these studies cells were incubated with 1µg/mL mAb for 30 minutes prior to radiation and this concentration was maintained in culture media for the duration of the experiment. Data are displayed as mean percent survival from 6 independent measures +/- standard error. Flow cytometry performed on cultured **C)** B78 or **D)** NXS2 cells that had been radiated *in vitro* 7 days prior with 12 Gy demonstrated no appreciable change in the surface expression of GD2. Mice bearing macroscopic syngeneic B16 melanoma tumors, which lack GD2 expression, were treated with 12 Gy radiation on day 1 and daily IT injection on days 6-10 of human IgG, hu14.18K322A, or hu14.18-IL2. In this tumor model, compared to control IgG, hu14.18K322A and hu14.18-IL2 did not significantly (NS) impact **E)** tumor response or **F)** animal survival. The number of animals per group (n) is indicated. **G)** *In vitro* clonogenic assays demonstrated no significant impact of hu14.18-IL2 on the intrinsic sensitivity of B78 cells to radiation (*p* = 0.670). Cells were incubated with 1µg/mL IC for 30 minutes prior to radiation and this concentration was maintained in culture media for the duration of the experiment. Data are displayed as mean percent survival from 6 independent measures +/- standard error.

**Supplemental Figure 5. *Immunohistochemistry demonstrates impact of radiation and immunocytokine injection on tumor infiltration by NK and CD8 and CD4-positive T cells.*** Immunohistochemistry was performed on tumors harvested 12 days after radiation for the **A**) NK cell marker NKG2A/C/E and for the T cell markers **B**) CD8 and **C**) CD4**.** Representative digital images taken at low (10x) magnification are shown. Positively stained cells were quantified and the results of this are displayed in Figure 4A-C.

**Supplemental Figure 6. *The time-sensitivity of combined radiation and hu14.18-IL2 is not observed with radiation and hu14.18K322A and radiation induces a dose-dependent increase in Fas/CD95 expression.* A)** Hu14.18K322A administration on days 6-10 is no more effective than administration on days 1-5 following radiation, in contrast to observations with combined radiation and hu14.18-IL2 (Figure 6A). \*\* *p* < 0.01, NS = non-significant (*p* ≥ 0.05). **B**) Plasma membrane expression of Fas/CD95 increases following *in vitro* radiation of cultured B78 cells in a dose-dependent manner. A fitted polynomial curve (dashed line) suggests a sigmoidal dose response curve. All cells were radiated 7 days prior to flow cytometry in this assay. Time appears to be a critical factor in the induction of Fas/CD95 expression (Figure 6C) whereas **C**) dose fractionation did not have a marked impact. Fractionated radiation was delivered once daily and initiated seven days prior to flow cytometry (day -7). For **B**) and **C**) results of triplicate experiments are displayed as means +/- standard error.