Supplementary Figure 1: Polyclonal ROR1 antibody binding domain diminishes subsequent binding with ROR1 monoclonal antibody epitope 2A2. Antibody competitive binding assay showing results from $ROR1^+$ Mino, JeKo-1 cells and $ROR1^-$ MEC1 cells. Cells are each pre-incubated with either an unlabeled polyclonal ROR1 antibody, a random sequence polyclonal isotype control, or no block. Cells are then probed with fluorescence conjugated monoclonal ROR1 antibody (2A2-PE) indicated below the X-axis legends. *$p<0.05$. n=3 independent experiments.

Supplementary Figure 2: Flow cytometry analysis of ROR1 expression on surface of $ROR1^+$ (HG3, 697, Mino, and JeKo-1) cell lines and $ROR1^-$ (MEC1) cell line. Cell lines were stained with PE-conjugated polyclonal ROR1 antibody. *$p<0.05$

Supplementary Figure 3: HuXBR1-402-G5-PNU is not cytotoxic towards $ROR1^-$ ALL cell line, REH. Dose response of $ROR1^-$ pre-B cell ALL cell line REH to huXBR1-402-G5-PNU (red line) and trastuzumab-G5-PNU (black line) treatment. IC50 + 95% Confidence interval are as follows, huXBR1-402-G5-PNU— 7182ng/mL [5853, 8811]; trastuzumab-G5-PNU— 4568ng/mL [4240, 4923]. Viability was measured using MTS assays and relative light units (RLU) values for each dose were generated after 72 hour treatment in two independent experiments.

Supplementary Figure 4: Direct cytotoxicity with huXBR1-402-G5-PNU (10ug/mL) at 24 and 96 hours. Direct cytotoxicity assay on ROR1+ MCL cell lines, JeKo-1 and Mino, ALL cell line, 697, and ROR1- CLL cell line MEC1. 2.5x105 plated cells were treated with 10ug/mL of

relevant antibodies and controls. Normalized viability (to vehicle) is reported as measured by Annexin V/ propidium iodide staining after 24 or 96 hours of culture. n= at least 3 independent experiments.

Supplementary Figure 5: HuXBR1-402-G5-PNU is not specifically cytotoxic towards ROR1$^-$ AML cell lines. (A) ROR1 surface expression on AML cell lines. (**B)** Direct cytotoxicity assay on ROR1$^-$ AML cell lines, KG1a, MOLM13, MV411, OCI-AML, U937, and HL60. 2.5x10^5 plated cells were treated with 10ug/mL of relevant antibodies and controls. Viability is reported as measured by Annexin V/ propidium iodide staining after 72 hours of culture. No difference is seen between huXBR1-402-G5-PNU compared to trastuzumab-G5-PNU treatment due to nonspecific FC mediated phagocytosis of both conjugated antibodies by AML cell lines

Supplementary Figure 6: Representative flow analysis of human ROR1 surface expression on CD5$^+$/CD19$^+$ B cells from huROR1-TCL1 splenocytes. Schematic shows representative flow analysis of thawed huROR1-TCL1 splenocytes before engraftment. >80% of all cells are leukemic CD5$^+$/CD19$^+$ B cells of which >90% express human ROR1 on the surface. Human ROR1 positive gate was set based on isotype antibody staining.

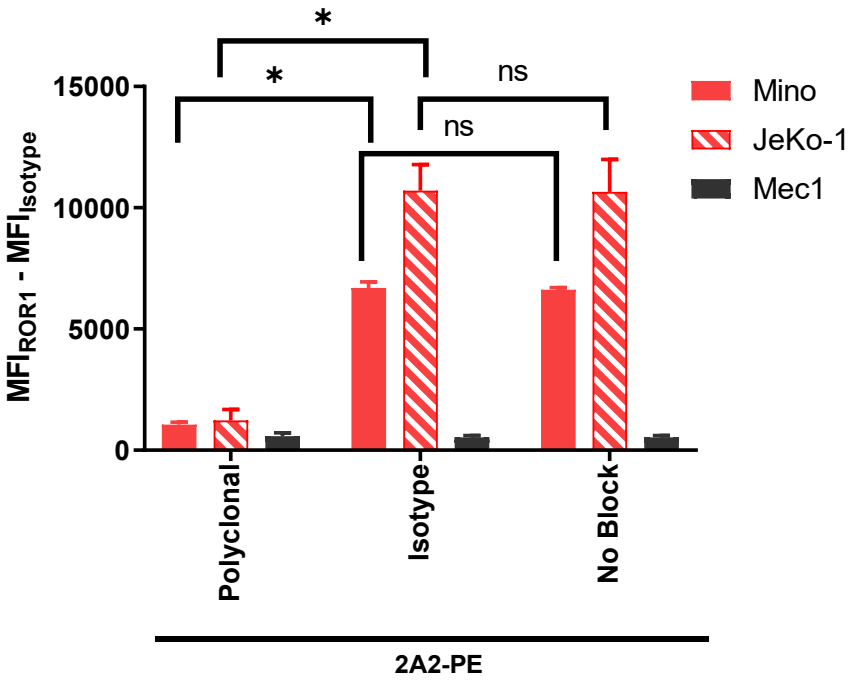
Supplementary Figure 7: HuXBR1-402-G5-PNU suppresses tumor growth in huROR1-TCL1 leukemia engrafted mice (repeat cohort). Weekly peripheral leukemia cell counts of second independent mouse cohort from Figure 4C as determined by flow cytometry. Mice were engrafted with 5×10^6 huROR1-TCL1 spleen-derived leukemic cells via tail vein injection. All mice were treated with 1mg/kg of either huXBR1-402-G5-PNU, Trastuzumab-G5-PNU, or equal

volumes of vehicle three times per week for one week after enrollment criteria was met (peripheral leukemia proportion was greater than 5% of total white blood cells). n= 5 mice per group

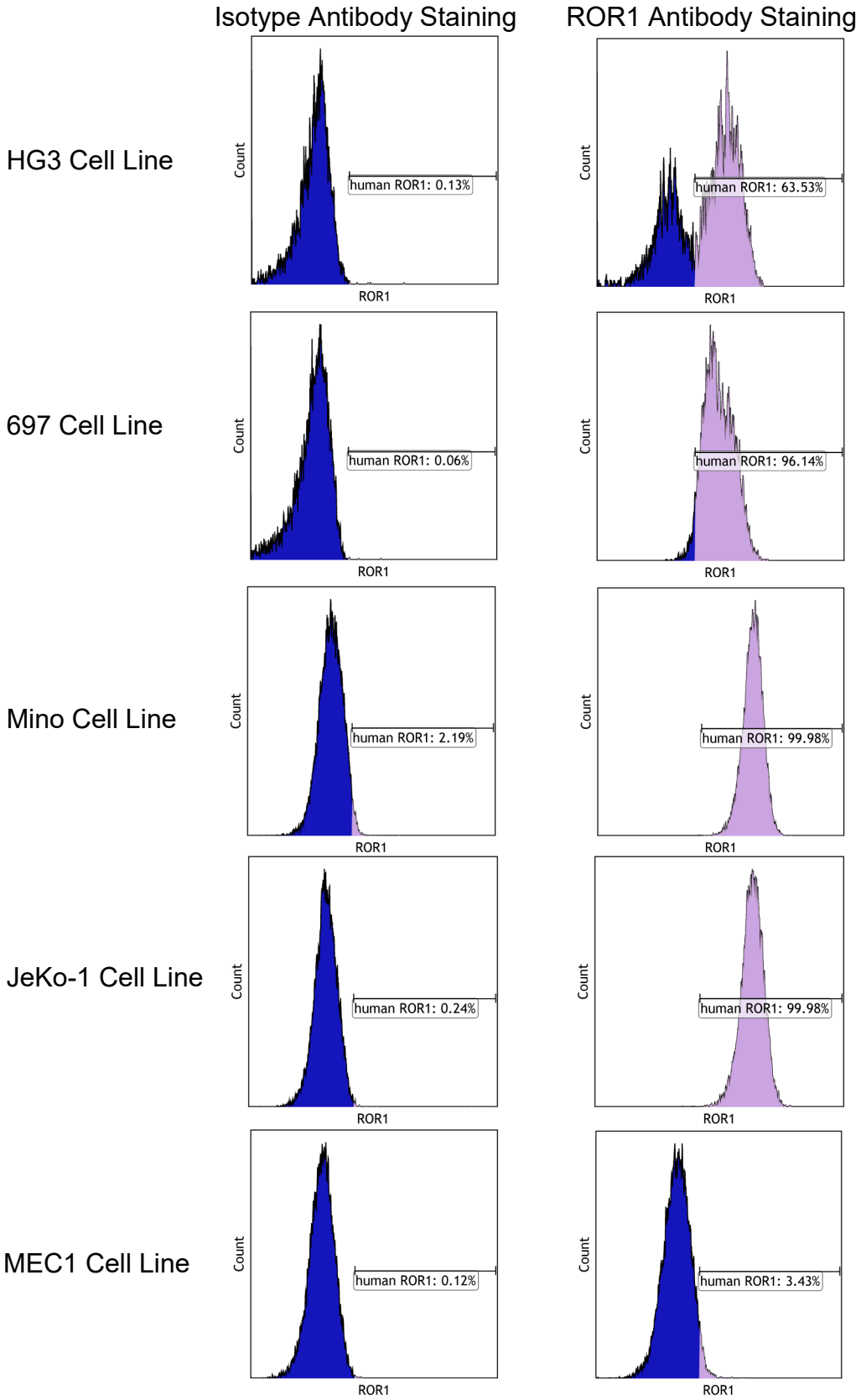
Supplementary Figure 8: Supplementary Figure 8: Venetoclax sensitivity and synergy with huXBR1-402-G5-PNU. (A) EC50 of Mino cells treated with venetoclax. (B), (C) Venetoclax EC50 for JeKo-1 and HG3 cell lines on left most panel. Matrices on right side shows results of MTS synergy assays with venetoclax and huXBR1-402-G5-PNU or isotype control trastuzumab-G5-PNU based on the Loewe additivity scores (blue colors represents presence of synergy while red colors represents antagonism; green represents non-additive and non-antagonistic combinations). n= 3 independent experiments for all experiments.

Supplementary Figure 9: ROR1 surface expression is maintained in BCL2 overexpressing 697 cell lines and abrogates cytotoxicity of huXBR1-402-G5-PNU. (A) Flow cytometry analysis of ROR1 surface expression on BCL2 overexpressing 697 cell lines. **(B)** Uncropped western blot analysis of BCL2 protein levels in parental and BCL2 overexpressing 697 cell lines showing almost 10-fold increase in BCL2 protein levels. In lanes 1 and 3 are parental 697 cells and in lane 2 is the BCL2 overexpressing 697 cell line. (C) Direct cytotoxicity assay on ROR1 + ALL cell line 697 and the corresponding BCL2 overexpressing 697 cell line. $2.5x10^5$ plated cells were treated with 10ug/mL of relevant antibodies, controls, or 10nM venetoclax as labeled. Viability is reported as measured by Annexin V/ propidium iodide staining after 72 hours of culture.

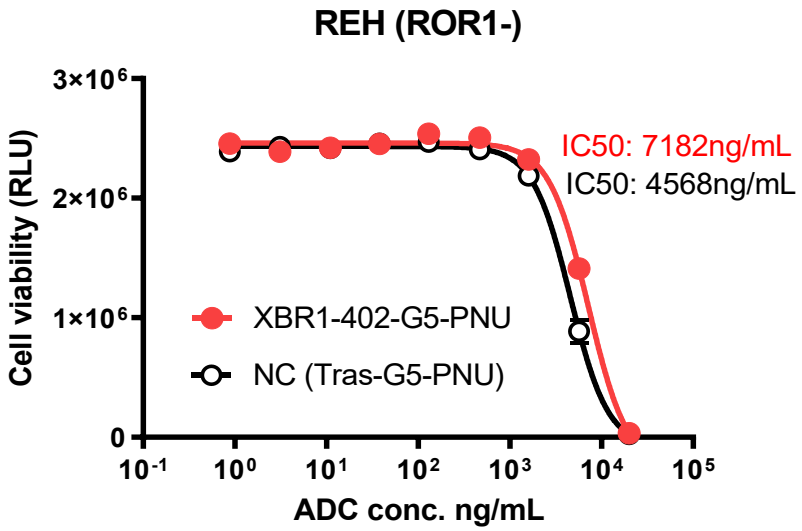
Supplementary Figure 1: **Polyclonal ROR1 antibody binding diminishes subsequent binding with ROR1 monoclonal antibody epitope 2A2.**



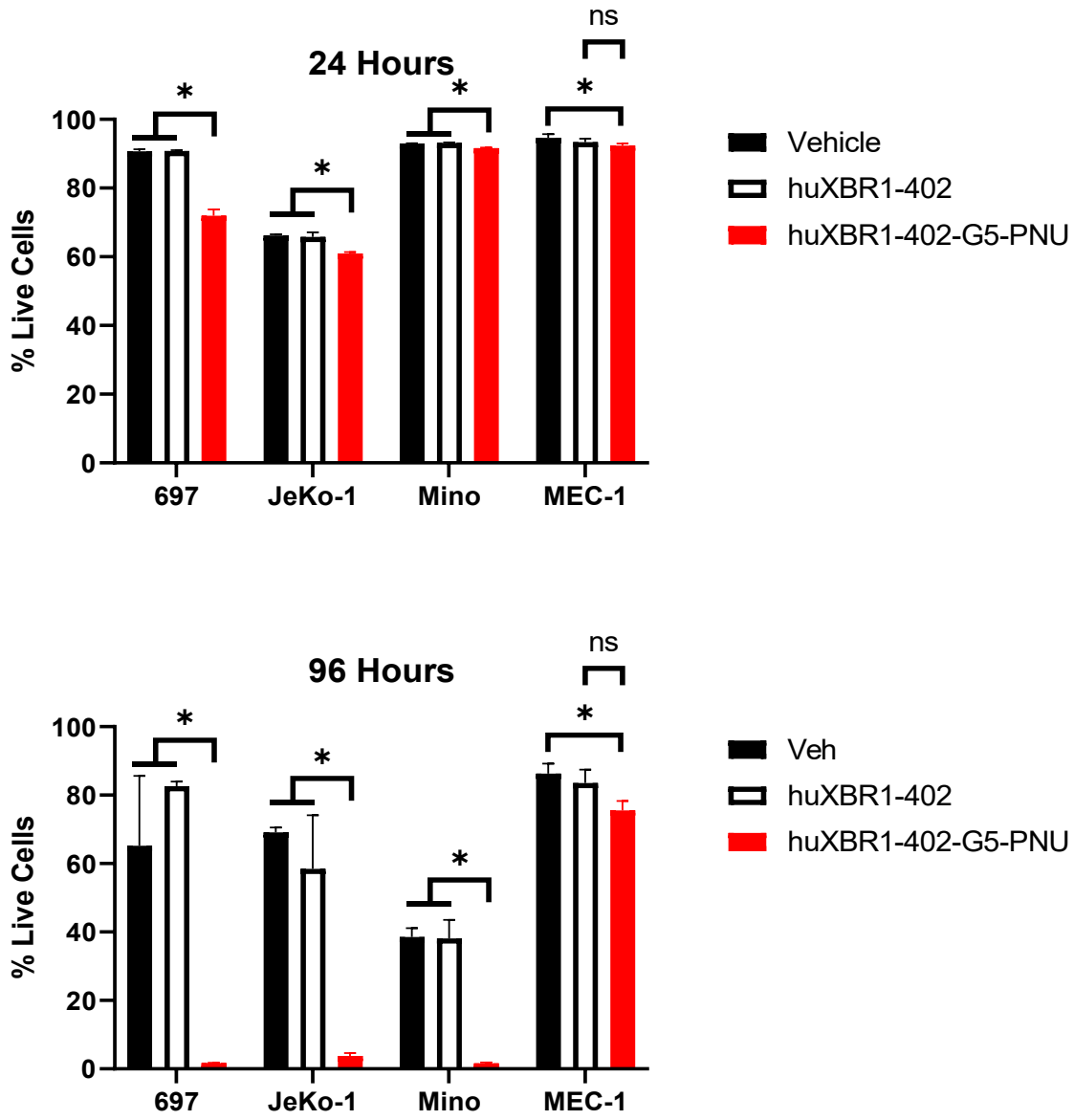
Supplementary Figure 2: **Flow cytometry analysis of ROR1 expression on surface of ROR1^{+} (HG3, 697, Mino, and JeKo-1) cell lines and ROR1^{-} (MEC1) cell line.**



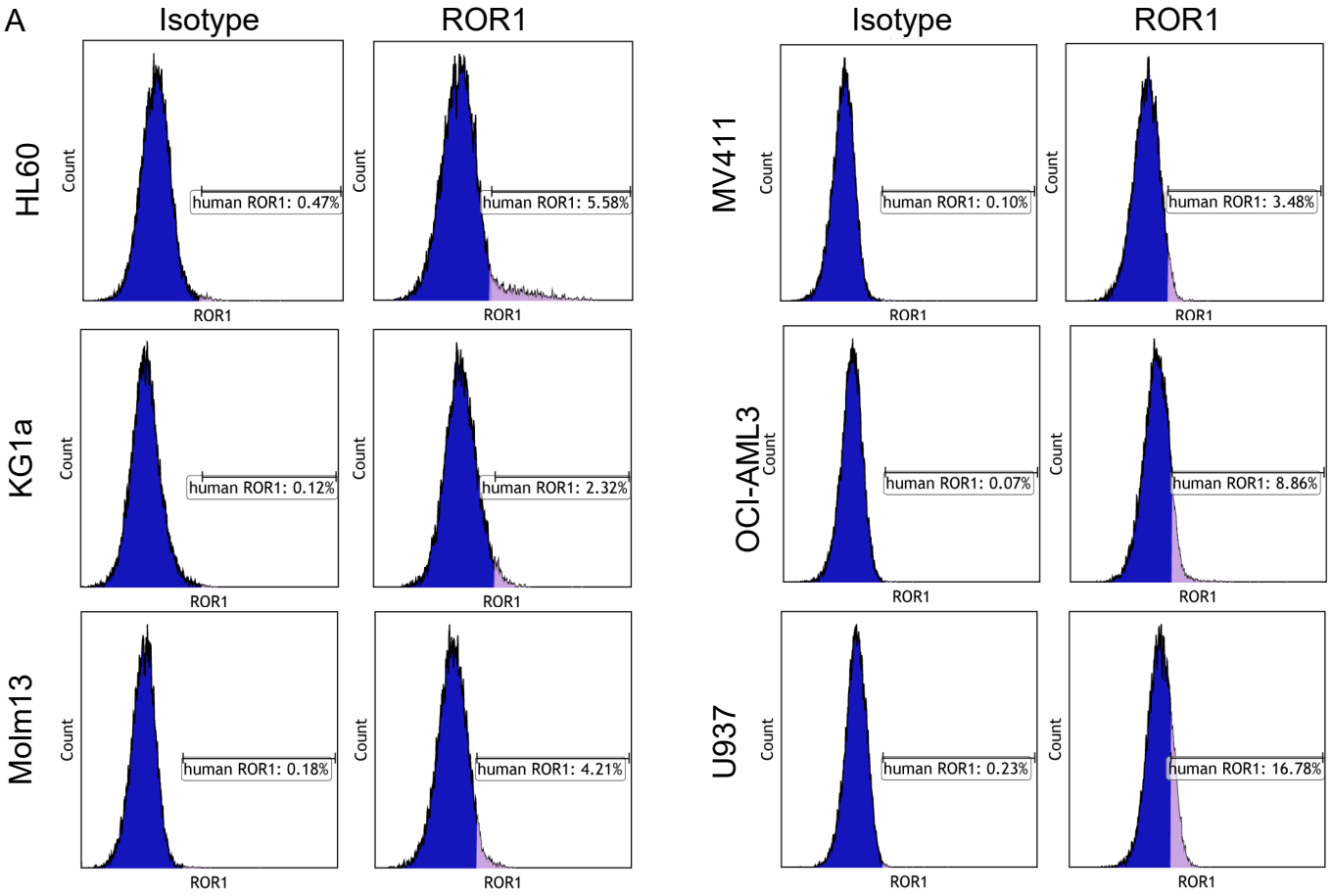
Supplementary Figure 3: **HuXBR1-402-G5-PNU is not cytotoxic towards ROR1⁻ ALL cell line, REH.**

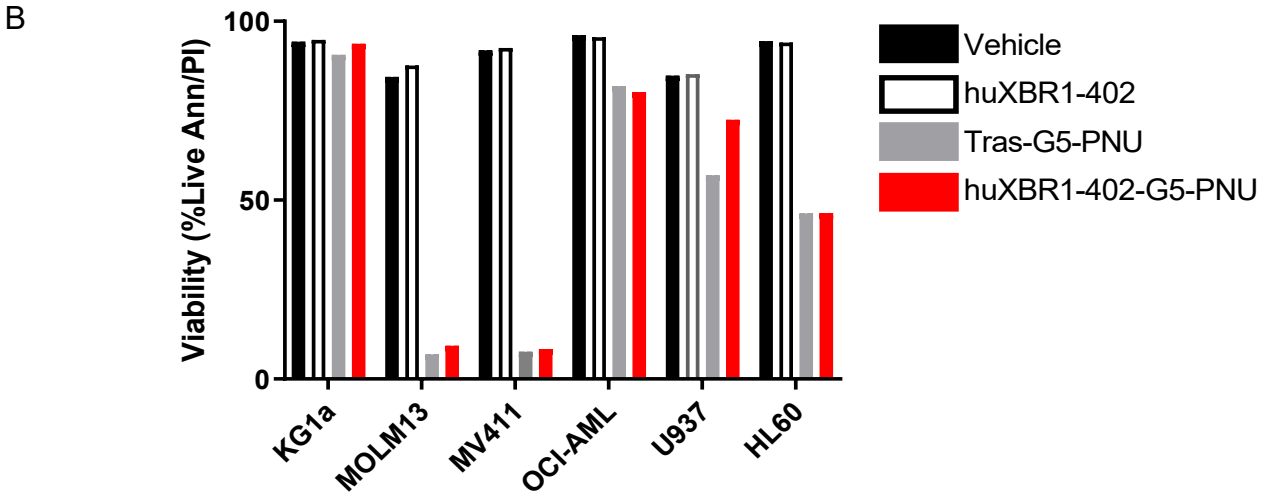


Supplementary Figure 4: **Direct cytotoxicity with huXBR1-402-G5-PNU (10ug/mL) at 24 and 96 hours.**

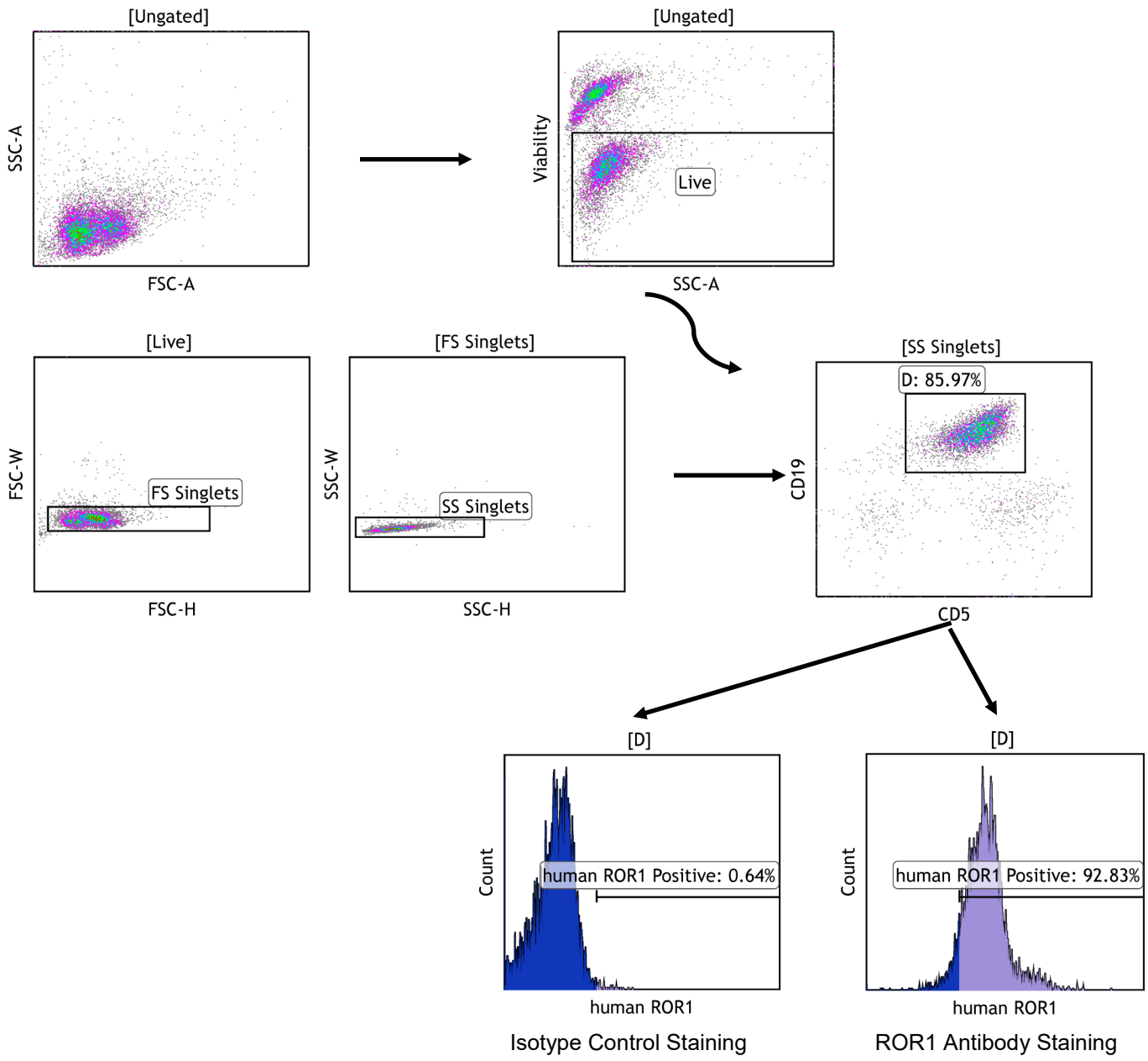


Supplementary Figure 5: **HuXBR1-402-G5-PNU is not specifically cytotoxic towards ROR1⁻ AML cell lines.**

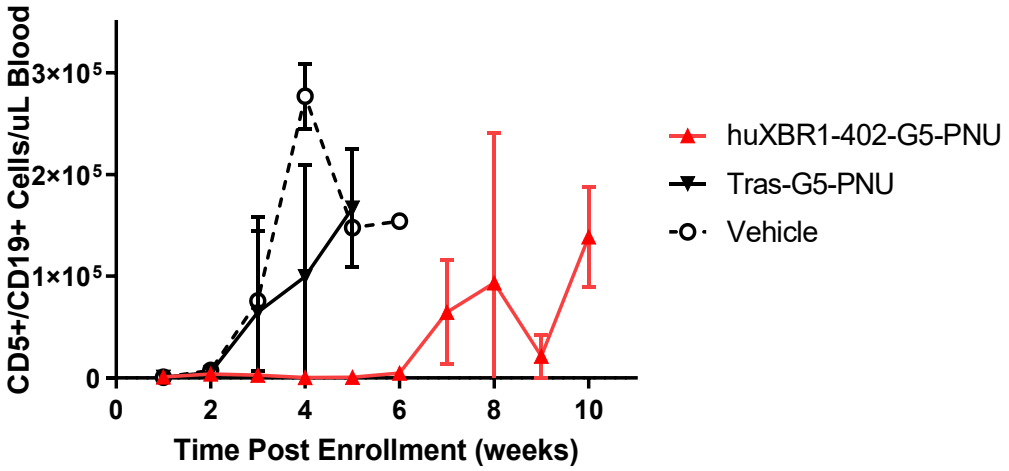




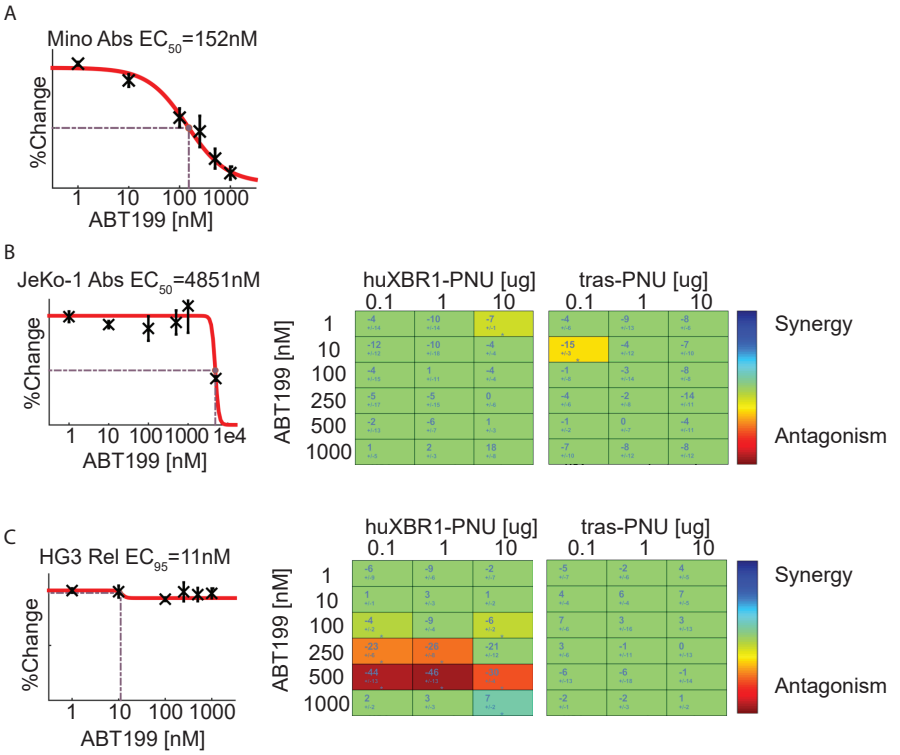
Supplementary Figure 6: **Representative flow analysis of human ROR1 surface expression on $CD5^{+}/CD19^{+}$ B cells from huROR1-TCL1 splenocytes.**



Supplementary Figure 7: **HuXBR1-402-G5-PNU suppresses tumor growth in huROR1-TCL1 leukemia engrafted mice.**



Supplementary Figure 8: Venetoclax sensitivity and synergy with huXBR1-402-G5-PNU



Supplementary Figure 9: ROR1 surface expression is maintained in BCL2 overexpressing 697 cell lines and abrogates cytotoxicity of huXBR1-402-G5-PNU