Supplemental Methods

Fluorophore conjugation of antibodies and antibody drug conjugates

Fluorophore-labeled antibodies were conjugated in-house. Briefly, mAbs in PBS were supplemented with 5% (v/v) 1M Borate Buffer pH 8.5, NHS ester-fluors were solubilized in DMSO at a concentration of 2mg/mL and added at a molar ratio of 10:1 fluor to mAb, then incubated at room temperature until the desired degree of labeling was obtained. Labeling was quenched with 1M Tris buffer pH 8.0 and labeled mAbs were desalted back into PBS via ZebaSpin 7K MWCO desalting columns. Concentration and degree of labeling were estimated by UV/Vis according to the manufacturer's instructions.

Generation of CD19 over-expression cell lines

Cells stably expressing human or cynomolgus CD19 orthologues were generated by lentiviral transduction. Briefly, lentiviral particles were produced according to the following protocol. 293T cells were plated on 10 cm tissue culture plates in DMEM + 10% FBS and allowed to reach ~90% confluence the next day. The cells are transfected by mixing 5 µg transfer plasmid, 6 µg packaging plasmids (TR30037P5, Origene) and 33 µL of Mirus TransIT Reagent (MIR 2700, Mirus). The transfer plasmid is a bicistronic lentiviral vector (CD513B-1, System Biosciences) containing the following ORF sequences: human CD19 (NM_001770.5) or cynomolgus CD19 (XM_005591541.2). The DNA mixture is then incubated for 30 minutes and then added dropwise onto 293T cells. The lentiviral particles are collected after 48 hours and 72 hours of transfection. The lentiviral particles are cleared by centrifugation and concentrated by Lenti0X concentrator (631232, Takara).

To engineer stable cell lines, cells were transduced with 50 µL of concentrated lentiviral particle in 10 µg/ml polybrene (TR-1003-G, Thermo Fisher Scientific). The cells are transduced and then selected with 2 µg/ml puromycin (A1113803, Thermo Fisher Scientific). The expression levels of the constructs were evaluated by GFP expression via flow cytometry.

Generation of Glucocorticoid Response Element (GRE) Reporter Cell Lines

The K562 GRE luciferase reporter cell line was generated at AbbVie and have been used to assess GR activation in structural-activity relationship (SAR) studies for other GRM ADCs.[1,2] The K562 cells have been transfected with human CD19 (detail described below) for the analysis of ABBV-319-induced GR activation. Briefly, K562 cells were seeded onto 6-well dish (3516, Costar) with 2 mL of complete growth medium [RPMI supplemented with L-Glutamine (11835-030, Thermo Fisher Scientific), 10% FBS (26140-079, Thermo Fisher Scientific), 1% Na Pyruvate (11360-070, Thermo Fisher Scientific) and 1% MEM NEAA (111140-50, Thermo Fisher Scientific)] at 500,000 cells per well for 24 hours at 37°C and 5% CO_2. On the next day, 1.5 µg of pGL4.36 [Luc2P/MMTV/Hygro] (E316, Promega), and 3 µL of PLUS reagent (10964-021, Thermo Fisher Scientific) were diluted into 244 µL Opti-MEM (31985-070, Thermo Fisher Scientific) and incubated at room temperature for 15 minutes. After incubation, diluted DNA solution was pre-incubated with 1:1 Lipofectamine LTX solution (94756, Thermo Fisher Scientific) (13.2 µL + 256.8 µL Opti-MEM) and incubated at room temperature for 25 minutes to form DNA-Lipofectamine LTX complexes. After incubation, 500 µL of DNA-Lipofectamine complexes were added directly to the well containing cells. K562 cells were transfected for 24 hours at 37°C and 5% CO_2. After

incubation, cells were washed with 3 mL of PBS and selected with complete growth medium containing 125 µg/mL of hygromycin B (10687-010, Thermo Fisher Scientific) for two weeks.

K562 pGL4.36[Luc2P/MMTV/Hygro] cells were harvested and seeded into a 15-mL conical tube (3516, Costar) with 1 mL of complete growth medium (RPMI + L-Glu, 10% FBS, 1% Na Pyruvate and 1% MEM NEAA) at 250,000 cells per well. 3 µg of human CD19 (RC230267, Origene) and 3 µL of PLUS reagent (10964-021, Thermo Fisher Scientific) were diluted into 244 µL Opti-MEM (31985-070, Thermo Fisher Scientific) and incubated at room temperature for 5 minutes. After incubation, diluted DNA solution was pre-incubated with 1:1 Lipofectamine LTX solution (94756, Thermo Fisher Scientific) (11µL + 239µL Opti-MEM) and incubated at room temperature for 15 minutes to form DNA-Lipofectamine LTX complexes. Subsequently, 500 µL of DNA-Lipofectamine complexes were added directly to conical tube containing cells. The cells and DNA-lipofectamine were mixed and seeded into a 6-well dish (3516, Costar) and incubated for 24 hours at 37°C and 5% CO_2. After 24-hour incubation, the cells were selected with 2 ml complete growth medium containing 125 µg/mL of hygromycin B (10687-010, Thermo Fisher Scientific) and 225 µg/mL G418 (10131-027, Thermo Fisher Scientific) for two weeks.

Internalization assays

One million viable cells were plated onto 96-well U-bottom plates (Corning) and blocked with 5% normal human serum (Sigma-Aldrich) on ice for 30 minutes. After three washes, the cells were stained with 70 nM Lysotracker (Thermo Fisher Scientific) in staining buffer (PBS + 2% FBS) for 1 hour at 37˚C. The cells were washed and subsequently stained with Alexa Fluor® 647

labeled ABBV-319 for 1 hour one ice. A portion of cells were removed for t=0h imaging while other cells were chased at 37˚C for 24 hours before imaging on Amnis ImageStream (Luminex).

Immunoblot detection

After transfer, the membranes were incubated with primary antibodies at the manufacturer's suggested concentration at 4ºC overnight. The primary antibodies used in this study include antibody to phospho-AKT Ser473 (4060, Cell Signaling Technology), BIM (2933, Cell Signaling Technology), PARP (9532, Cell Signaling Technology), Caspase-3 (9662, Cell Signaling Technology), and GAPDH (97166, Cell Signaling Technology). The membranes were washed three times with 1x PBST (9809, Cell Signaling Technology) and subsequently incubated with Peroxidase AffiniPure Goat Anti-Mouse IgG (H+L) (115-035-003, Jackson ImmunoResearch Laboratories) or Peroxidase AffiniPure Goat Anti-Rabbit IgG (H+L) (111-035-003, Jackson ImmunoResearch Laboratories) for 1 hour at room temperature. The membranes were washed three times with 1x PBST and then incubated with Pierce™ ECL Western Blotting Substrate (Thermo Fisher Scientific, cat# 32106). The membranes are then detected with Azure Image Systems C600.

RNA-seq analysis

FASTQ files were aligned to hg38 using STAR and then quantified for gene and transcript reads counts using Salmon, using the reference transcriptome of Ensembl v93. The MultiQC workflow was conducted to ensure the reads and alignment quality. For treatment conditions of each cell line, differential expression analysis was performed using edgeR R package. Meta-analysis was

performed across cell lines using MetaVolcanoR R package. Pathway enrichment analysis was performed using GSEA and clusterProfiler R packages. The glucocorticoid response gene signature using published gene set was computed using ssGSEA method. All plots were generated using ggplot2 or pheatmap packages.

CITE-seq analysis

CITE-seq FASTQ files were processed using cellranger FeatureBarcoding workflow to align reads for both RNA and protein. The majority of analysis was performed using Seurat V3. QC filtering kept cells with > 200 gene quantified and mitochondrial gene ratio < 15%. Protein assay data was additional quality controlled and normalized using dsb package. Doublets were identified leveraging PBMC lineage marker specificity and removed. Data across different samples were integrated using Seurat data integration workflow and performed for RNA and protein assay separately. Joint clustering of RNA and protein was conducted using Seurat FindMultiModalNeighbors function. After clustering and analysis of cluster markers by differential expression, cell types were predicted by projecting to human PBMC reference dataset. Further downstream data analysis and visualization were conducted using Seurat or ggplot2. Gene signature score of glucocorticoid response genes was computed using CelliD.

Cell cycle analysis

One million cells were resuspended in HBSS containing 2% FBS and ice-cold 70% ethanol were added in a dropwise manner to fix the cells. The cells were incubated on ice for at least 2 hours.

After brief wash, cells were resuspended in DAPI working solution (0.1% Triton X-100 and 10 µg/ml DAPI) and analyzed on the flow cytometer.

Mouse Pharmacokinetics Study

Whole blood samples diluted 1:5 in Meso Scale Discovery (MSD) assay buffer with EDTA were analyzed for ABBV-319 in a total anti-human MSD assay with electrochemiluminescent detection. Total antibody was analyzed by employing a goat anti-human IgG Fc Biotin and a goat anti human IgG Sulfo-Tag™ detection. ABBV-319 was used for the construction of the standard curves.

In the assay, samples were analyzed at a 1% final serum concentration. MSD standard curve fitting and data evaluation was performed using XLfit4 software (Version 5.5.0). Calibration curves were plotted from MSD luminescence units versus theoretical standard concentrations. A four-parameter logistic model was used for curve fitting. The regression equation for the calibration curves was then used to back calculate the measured concentrations. The linear range of the total assay was 0.031-7.5 µg/mL, with a lower limit of quantitation (LLOQ) of 0.031 µg/mL. Plates were considered valid when at least two-thirds of the QCs were within 30% of the expected values.

In Vivo Pharmacodynamic Analysis

RNA expression was determined using TaqMan® Gene Expression quantitative real-time PCR assay (Thermo Fisher Scientific Inc. Catalog Number: 4331182) for the genes FKBP5, TSC22D3

(GILZ), and ZBTB16 (Assay IDs: Hs01561006_m1, Hs00608272_m1, and Hs00232313_m1, respectively).

ADCP Assay

The activity of ABBV-319 on antibody dependent cellular phagocytosis (ADCP) by human macrophage is determined as described herein.

Human monocytes (STEMCELL Technologies) were differentiated into macrophages for 8 days in RPMI-1640 containing 10% FBS and 50 ng/ml of recombinant human M-CSF (BioLegend). Fully differentiated macrophages were detached from flasks to be co-cultured with target cancer cells for phagocytosis assays.

The human Non-Hodgkins Lymphoma cell line Raji and NU-DHL-1 expressing endogenous CD19 were selected as target cells. After washing with PBS, the target cancer cells were labeled with 5 µM of CFSE dye solution (Thermo Fisher Scientific) for 15 min, then co-incubated with human macrophage at 1:1 ratio. Isotype and CD19-targeting antibody and antibody drug conjugate was added at selected concentrations. After co-culture for 3 hours at 37°C, cells were harvested, washed and stained with a macrophage maturation marker, Alexa Fluor 647 labeled CD68 antibody (BioLegend), followed by flow cytometry analysis.

The phagocytosis index representing the population percentile of phagocytosing macrophages was calculated by counting $CFSE^{+}CD68^{+}$ double positive macrophages among total CD68+ macrophages.

CDC assay

Lymphoma cells were plated at $1.25x10^{5}$cells per well on a 96-well plate (3903, Corning) and treated with 100 nM of antibody and ADCs for 30 minutes at 37°C. At the end of incubation, gender unspecified, pooled not filtered, complement preserved human serum (HUMANSRM-0102105, BioIVT) is added to yield a final serum concentration of 5% and to serve as the complement source. The cells were incubated for 3 hours at 37°C and then CellTiter-Glo (G7573, Promega Corporation) reagent is added to assess cell viability. Luminescent intensity was measured with VICTOR3 Multilabel Plate Reader (Perkin Elmer). Cell viability was plotted using GraphPad Prism.

In Vitro ADCC assay

The ADCC Reporter Bioassay (V and F variants; G7010 and G9790, Promega) were performed according to the manufacturer's protocol with minor modifications. Briefly, the target cell line Raji was plated in 5 µL of ADCC assay buffer (RPMI media containing 4% low IgG serum) at 2500 cells per well. The antibody was titrated in ADCC assay buffer and 5 µL were added at indicated antibody concentration. Effector cells from the V Variant and F Variant kits were resuspended in ADCC assay buffer and added at 5 µL per well to achieve effector to target cell ratio (E:T) of 6:1. The target cell-antibody mixtures were incubated with effector cells expressing V variant and F

variant at 37°C for 6 hours and 24 hours, respectively. At the endpoint, 15 µL of Bio-Glo Luciferase Reagents were added and luciferase activity were measure with Molecular Devices SpectraMax M5 plate reader.

PBMC co-culture ADCC assays were performed as described below. The target cell lines (RS4;11, Raji and KARPAS422) were washed with PBS and labelled with 1 µM CFSE in PBS (C34554, Thermo Fisher Scientific) for five minutes at 37°C. The labelled target cells were then washed three times with media containing 10% FBS. 20,000 labeled target cells in 50 µL are plated onto V-shaped 96-well plates. Antibodies and ADCs were titrated in culture media and 10 µL were added to achieve indicated final concentrations. PMBC from normal donor (AllCells) were added in 40 µL at effector to target cell ratio of 20:1 and the cells were incubated at 37°C for four hours. After the incubation, the cells are washed once with PBS and stained with Live/Dead Fixable Violet Dead Cell Stain Kit (L34955, Thermo Fisher Scientific) for 30 minutes at room temperature and then wash once with 200 µL ice-cold PBS. Cells are fixed with 4% paraformaldehyde in PBS for 15 minutes and then wash once with 200 µL PBS. The fixed cells are resuspended in 100 µL PBS and store in 4°C until analysis on Stratedigm S1000EON flow cytometer. The CFSE-labeled target cells were gated, and the percentage of dead (Live/Dead Violet dye-positive) cells were captured. The % specific lysis was calculated by subtracting the percentage of dead cells in each treated condition with the untreated control containing only effector and target cells.

Flow cytometry immunophenotyping

Immunophenotyping of blood samples was performed using high dimensional flow cytometry. 20 µL of whole blood was drawn at specific intervals prior to and throughout the treatment schedule and placed into a well of a 96-well plate. RBCs were lysed using 100 µL of ACK lysis solution (Thermo Fisher Scientific) for 2 minutes at room temperature, and then immediately quenched with 100 µL MACS Running Buffer ("MACS Buffer" - Miltenyi Bio) supplemented with 10% FBS. Quenched samples were centrifuged at 400 x g for 5 minutes and then washed with 200 µL PBS to remove serum proteins. Pellets were resuspended in 50 µL of a 1:100 dilution of LIVE/DEAD Fixable Blue Dead Cell Stain (Thermo Fisher Scientific) in PBS and stained for 10 minutes on ice. Samples were preserved using 70 µL of proteomic stabilization buffer (Smart Tube Inc.) added directly to the 50 µL sample and incubated for 10 minutes at room temperature. After the 10-minute incubation, the samples were placed directly into -80°C storage. All samples throughout the study were prepared in this manner, so that they could be stained and acquired in a single batch at the end of the study. After all samples had been processed and cryopreserved for at least 1 week, they were rapidly thawed and washed 2x with Thaw/Lyse Buffer and then 1x with MACS Buffer. Samples were stained for 30 minutes at 4°C with a cocktail of conjugated antibodies to identify various immune subsets including CD8 T cells and NK cells. The full list of antibodies including clone, fluor and dilutions can be found in Supplemental Table 3. Stained samples were washed 2x with MACS buffer, fixed and permeabilized using the FoxP3 Transcription Buffer set (Thermo Fisher Scientific) according to the manufacturers protocol. Permeabilized samples were stained for intracellular targets overnight at 4°C, washed with Perm/Wash buffer, and resuspended in a final volume of 100 µL prior to being acquired on a BD Fortessa cytometer (standard 5-Laser configuration). Analysis of

the FCS files was done in OMIQ using a hierarchical gating strategy that included gates on live cells, single cells, and human CD45+ cells. Percent B cells (CD20+ and CD19+) was calculated based on total human CD45+ cells present whereas percent T cells (CD3+, CD56-) and percent NK cells (CD3-, CD56+) were calculated based on the total number of human CD45+ cells minus the number of B cells. Since the depletion of B cells was obvious among the treatment groups, the frequency of all other populations would be artificially high based on total CD45+. Thus, the B cell component was removed from these measurements to assess whether they were changing in frequency.

CD19 Receptor Quantification by Flow Cytometry

Cell lines were stained with a CD19-PE antibody (clone HIB19; Thermo Fisher Scientifc) to assess antigen copy number. Samples were first stained for viability using the Fixable LIVE/DEAD NIR stain, (Thermo Fisher Scientific) followed by an 8-point two-fold serial dilution with a top concentration of 2 μg/mL on each line to ensure receptor saturation. Samples were stained on ice for 30 minutes, washed 2x with MACS Buffer, and then acquired on the Agilent Quanteon Flow Cytometer (standard configuration). Greater than 20,000 live single cells were collected. Using the same instrument setup, Quantibrite-PE beads were acquired according to the manufacturer's instructions (BD Biosciences). Samples were analyzed in OMIQ by gating on live, single cells, and then exporting the median fluorescence intensity (MedFI) of the PE channel for each. Quantibrite-PE MedFI values were used to create a linear regression line ($R^2 = 0.9997$), and MedFI values from saturating data points of each cell line's PE expression were plugged into the equation to yield a CD19 copy number for each cell line (supplemental Table 2).

GR Relative Expression via Flow Cytometry

Cell lines were stained for expression of the glucocorticoid receptor (GR). Harvested cell lines were stained using the LIVE/DEAD NIR viability stain for 15 minutes and then washed with MACS Buffer. Cell pellets were resuspended in 100 µL of freshly prepared 4% paraformaldehyde and incubated at room temperature for 15 minutes. Samples were washed 2x with MACS buffer and resuspended in the residual volume. They were permeabilized by slowly adding 200 µL of ice-cold 90% methanol and incubated for 20 minutes at -20°C. Permeabilized samples were washed and stained with anti-GR Alexa Fluor 488 (Cell Signaling Technologies) antibody for 30 minutes. Finally, samples were washed 2x with MACS, and 20,000 live, single events were acquired on the Quanteon. In OMIQ, live, single cells were gated and then Alexa Fluor 488 channel MedFI values were exported for each sample. A GR knockout cell line was used as a negative control. Each cell line was run with and without GR staining but processed the same in all other regards. To normalize the impact of autofluorescence of the various cell lines, a fold-change increase of GR stained over the paired unstained MedFI value was calculated. Next, the fold-change value of the GR knockout cell line was subtracted from the fold-change value of all the other cell lines to account for non-specific antibody background staining. The final fold change values are representative of normalized, background subtracted, fold-change values which can be interpreted as relative GR expression of the given cell line (supplemental Table 2).

Flow cytometric binding assays

Adherent cells were first detached by Versene solution (15040066, Thermo Fisher Scientific). Cells were washed with the FACS buffer (PBS + 2% FBS) and blocked with BD human Fc block (564219, BD Biosciences) at room temperature for 10 minutes. Cells were stained with Alexa Fluor 647-labelled antibody and ADC for 30-minute on ice. After washes, cells were stained with Live/Dead Fixable Violet Dead Cell Stain Kit (L34955, Thermo Fisher Scientific) according to the manufacturers' suggested protocol. Cells were then fixed with 4% paraformaldehyde in PBS for 15 minutes on ice. After washes, fixed cells were analyzed with BD FACSCanto flow cytometer.

Surface plasma resonance assay

Affinity of Af. CD19 mAb and ABBV-319 for FcγRIIIa (V158 and F158) were measured by Biacore-8K. Briefly, Anti-histidine antibody was immunobilized on CM5 chip via amine capture. Histidine-tagged FcγRIIIa (V158 and F158) were captured. Antibodies at various concentrations were then injected over the flow cell. After each injection of analyte, the chip surface was regenerated with 10 mM glycine-HCl, pH 1.5. Sensorgrams were fit with a 1:1 Langmuir binding model in Biacore T200 Evaluation Software.

References for Supplemental Methods

1. Hobson AD, McPherson MJ, Hayes ME, et al. Discovery of ABBV-3373, an Anti-TNF Glucocorticoid Receptor Modulator Immunology Antibody Drug Conjugate. *J Med Chem*. 2022;65(23):15893-15934.
2. Hobson AD, Xu J, Welch DS, et al. Discovery of ABBV-154, an anti-TNF Glucocorticoid Receptor Modulator Immunology Antibody-Drug Conjugate (iADC). *J Med Chem*. 2023;66(17):12544-12558.

Supplemental Table and Figure Legends

Supplemental Table 1. Cell lines from in the *in vitro* screen and their NHL subtypes and culture conditions

Supplemental Table 2. EC_{50} and E_{max} from the in vitro screen of GRM payload, prednisolone, dexamethasone, Isotype mAb ADC, Af. CD19 mAb, and ABBV-319 across malignant B-cell lines. CD19 and GR expression are displayed for each cell line.

Supplemental Table 3. Antibodies used for flow cytometric immunophenotyping, GR quantitation and GR expression analysis.

Supplemental Table 4. Equilibrium constant (K_D) from Surface Plasma Resonance (SPR)

Supplemental Figure 1. Species cross-reactivity of ABBV-319. (A-C) Flow cytometric binding analysis of Alexa Fluor 647-labeled antibody and ADC on parental 293T (A), 293T expressing human CD19 (B), and 293T expressing cynomolgus monkey CD19 (C). Means ± SEM are shown. (D-E) The activation of GRE reporter after treatment with indicated doses of ABBV-319 in K562 GRE reporter cell line over-expressed with human CD19 (D) or cynomolgus monkey CD19 (E). Means ± SEM are shown.

Supplemental Figure 2. Correlation analysis between EC50 and target expression. (A) A plot of GRM small molecule EC_{50} versus GR expression from flow cytometric analysis. (B) A plot of ABBV-319 EC50 versus GR expression from flow cytometric analysis. (C) A plot of ABBV-319 EC50 versus CD19 expression from flow cytometric analysis. (D) A plot of ABBV-319 EC50 versus CD19 expression from flow cytometric analysis with only the GRM-sensitive cell lines. Spearman correlation coefficients and p-values from the Spearman correlation analysis are shown.

Supplemental Figure 3. Signaling analysis of GRM/ABBV-319 resistant cell lines. (A) SU-DHL-4 cells were pre-treated with 100 nM Af. Isotype mAb or Af. CD19 mAb for an hour and then stimulated with 1 μg/ml anti-IgM for indicated time. Cell lysates were resolved on SDS-PAGE and immunoblot analysis for phospho-AKT (Ser473) and GAPDH are displayed. GAPDH is used as the loading control. (B) Immunoblot analysis of BIM, cleaved caspase 3, PARP and beta-actin after treating SU-DHL-8 with 10 nM GRM payload and 100 nM ABBV-319 for indicated time. SU-DHL-6 treated with 10 nM GRM for 48h were used as the positive control. (C) Cell cycle analysis of SU-DHL-8 after treatment with 10 nM GRM and 100 nM ABBV-319 for indicated time. The % of cells from sub-G1, G0-G1, S and G2-M phases of cell cycle are displayed.

Supplemental Figure 4. Supplemental data for the CDX *in vivo* data. (A) A table summarizing *in vivo* efficacy of ABBV-319 in different CDX models. The cancer indication for different CDX

models is shown. The maximal tumor growth inhibition (% TGI Max) and tumor growth delay (TGD) are displayed for single-dose 15 mg/kg of ABBV-319 treatment in NSG or CB17 SCID mice. (B) Growth of xenografted SUP-B15 tumors in NSG mice after indicated treatment regimen. SD denotes single dose. Means ± SEM of tumor volume were plotted for each treatment group versus days from randomization. (C) Growth of xenografted SU-DHL-6 tumors in SCID-beige mice after indicated treatment regimen. QD denotes daily treatment and SD denotes single dose. Means ± SEM of tumor volume were plotted for each treatment group versus days from randomization. (D) Total antibody detected in the mouse whole blood from the SU-DHL-6 study (C). Means ± SEM are shown.

Supplemental Figure 5. **ABBV-319 induces antibody-dependent cellular phagocytosis (ADCP) but not complement-dependent cytotoxicity (CDC).** (A-B) Fold change in phagocytic index compared to vehicle control are displayed for Raji (A) and NU-DHL-1 (B) cells after treatment with 200 nM of indicated agents in presence of *in vitro* differentiated macrophages. Mean ± SEM are displayed. (C) Phagocytic indexes are displayed for Raji after treatment with dose-titrated isotype-GRM ADC and ABBV-319. Means ± SEM are shown. Detailed protocols describing the ADCP assay and definition of phagocytic index are included in Supplemental Methods section. (D-F) Complement-dependent cytotoxicity assay after the treatment of Raji (D), Ramos (E), and SU-DHL-6 (F) with 100 nM of indicated agents in presence of complements for 3 hours. Means ± SEM are shown. Statistical significance is determined with one-way ANOVA, with Dunnett's multiple comparison test. ns, not significant. ****$p<0.0001$.

Supplemental Table 1

Cell Line	Cancer Type	Culture Media
SUDHL2	ABC DLBCL	IMDM + 10% HS
TMD8	ABC DLBCL	RPMI + 10% FBS + 1% pyruvate
U2932	ABC DLBCL	IMDM + 10% HS
OCI-LY3	ABC DLBCL	IMDM + 10% HS
HBL-1	ABC DLBCL	IMDM + 10% HS
Ri1	ABC DLBCL	IMDM + 10% HS
OCI-LY2	GCB DLBCL	IMDM + 10% HS
HT	GCB DLBCL	IMDM + 10% HS
SU-DHL-10	GCB DLBCL	IMDM + 10% HS
OCI-LY19	GCB DLBCL	IMDM + 10% HS
Sudhl-8	GCB DLBCL	IMDM + 10% HS
Pfeiffer	GCB DLBCL	IMDM + 10% HS
OCI-LY8	GCB DLBCL	IMDM + 10% HS
OCI-LY1	GCB DLBCL	IMDM + 10% HS
OCI-LY18	GCB DLBCL	IMDM + 10% HS
Karpas-422	GCB DLBCL	RPMI + 20% FBS
OCI-LY7	GCB DLBCL	IMDM + 10% HS
SU-DHL-6	GCB DLBCL	IMDM + 10% HS
SU-DHL-4	GCB DLBCL	IMDM + 10% HS
DB	GCB DLBCL	RPMI + 10% FBS
WSU-DLCL2	FL	RPMI + 10% FBS
DOHH-2	FL	RPMI + 10% FBS
SC-1	FL	RPMI + 10% FBS
REC-1	MCL	RPMI + 10% FBS
Granta-519	MCL	MEM + 10% FBS
Mino	MCL	RPMI + 20% FBS
Z-138	MCL	IMDM + 10% HS
JVM-2	MCL	RPMI + 10%FBS
Jeko	MCL	RPMI + 20% FBS
Farage	GCB DLBCL	RPMI + 20% FBS
Raji	BL	RPMI + 10% FBS
NU-DHL-1	GCB DLBCL	IMDM + 10% HS
RS4;11	ALL	RPMI + 10% FBS
SUP-B15	ALL	IMDM + 20 FBS

Supplemental Table 2

Cell Line	Cancer Type	CD19 Expression (ABC)	GR Expression	Rearrangement				GRM		Dexamethasone		Prednisolone		Isotype mAb		Af. CD19 mAb		ABBV-319	
				MYC	BCL 2	BCL 6	n	EC_{50} (μM)	E_{max} (%)	EC_{50} (μM)	E_{max} (%)	EC_{50} (μM)	E_{max} (%)	EC_{50} (μM)	E_{max} (%)	EC_{50} (μM)	E_{max} (%)	EC_{50} (μM)	E_{max} (%)
Raji	BL	27283.0	58.4				3	>0.1	57.4	>1	33.0	>10	34.7	>1	52.6	>1	18.7	>1	-8.5
HT	GCB DLBCL	35061.5	13.4				2	0.00033	31.7	0.008	30.9	0.13	28.7	> 1	16.9	> 1	2.5	> 1	16.9
Ri-1	ABC DLBCL	5161.6	1170.8	+ Non-IG		+	4	0.00089	34.5	0.062	36.5	1.42	41.4	> 1	0.2	> 1	8.5	> 1	36.5
Pfeiffer	GCB DLBCL	20356.0	32.7				4	0.00097	34.8	0.011	41.5	0.30	45.9	> 1	12.0	> 1	3.4	> 1	15.6
OCI-LY3	ABC DLBCL	1.0	37.4				2	0.00144	36.5	0.034	42.7	0.12	29.8	> 1	5.8	> 1	8.2	> 1	21.6
U-2932	ABC DLBCL	11037.4	307.3				4	0.00206	48.7	0.010	46.3	0.08	40.5	> 1	8.3	> 1	17.9	> 1	67.2
Sc-1	FL	4122.9	38.9	+ IG	+	+	2	> 0.1	-5.8	> 1	26.5	> 10	-23.5	> 1	16.4	> 1	26.8	> 1	36.0
WSU-DLCL2	FL	11706.8	36.9	+ Non-IG	+	+	2	> 0.1	-1.2	> 1	-3.5	> 10	-1.4	> 1	5.7	> 1	12.3	> 1	34.7
OCI-LY8	GCB DLBCL	38186.3	27.6	+ IG	+	+	2	> 0.1	26.3	> 1	31.4	> 10	18.7	> 1	34.9	> 1	58.7	> 1	32.9
SU-DHL-2	ABC DLBCL	12.1	2.8				2	> 0.1	9.1	> 1	10.0	> 10	1.1	> 1	4.1	> 1	0.9	> 1	14.5
SU-DHL-8	GCB DLBCL	23596.5	27.0				2	> 0.1	15.4	> 1	21.8	7.31	23.8	> 1	11.0	> 1	8.2	> 1	12.4
SU-DHL-4	GCB DLBCL	7835.7	43.2	+ Non-IG	+	+	2	> 0.1	7.2	> 1	9.1	> 10	6.8	> 1	16.1	> 1	5.3	> 1	10.2
Z-138	MCL	484.1	94.3				2	> 0.1	3.4	> 1	7.4	> 10	6.7	> 1	2.2	> 1	3.6	> 1	8.0
Granta-519	MCL	41118.9	464.0				2	> 0.1	-10.8	> 1	-7.4	> 10	-5.6	> 1	3.5	> 1	11.6	> 1	6.3
SU-DHL-10	GCB DLBCL	10813.9	278.7	+ IG	+		2	> 0.1	15.4	> 1	21.4	> 10	5.0	> 1	14.2	> 1	31.3	> 1	1.0
Mino	MCL	54656.4	164.0				2	> 0.1	-0.6	> 1	-1.8	> 10	1.8	> 1	5.0	> 1	2.8	> 1	0.7
RS4;11	ALL	113.9					2	0.10000	98.2					>1	0.5	>1	-2.3	0.82	95.5
Jeko-1	MCL	7490.0	17.7				2	0.00023	57.3	0.003	55.6	0.04	48.4	> 1	12.7	0.5	21.1	0.77374	54.3
OCI-LY18	GCB DLBCL	16498.3	55.1	+ IG	+		4	0.00087	53.4	0.009	55.9	0.17	56.1	> 1	5.9	> 1	8.6	0.65911	45.0
OCI-LY2	GCB DLBCL	29413.2	26.3				2	> 0.1	7.6	> 1	7.1	> 10	6.7	> 1	11.8	0.5	21.6	0.50023	24.5
REC-1	MCL	30832.1	8.4				2	0.00077	93.5	0.010	99.0	0.27	90.7	> 1	1.4	> 1	-2.9	0.34947	31.0
HBL-1	ABC DLBCL	1435.4	267.3				2	0.00041	76.9	0.006	82.9	0.05	76.3	> 1	8.3	> 1	11.9	0.34099	61.0
SUP-B15	ALL	109.3					2	0.089	98.4					>1	-0.4	>1		0.32	96.5
OCI-LY1	GCB DLBCL	11730.1	217.0				2	0.00155	75.4	0.019	77.5	0.20	74.2	> 1	19.1	> 1	12.1	0.27782	53.7
DoHH-2	FL	39106.2	155.5	+ IG	+		4	0.00018	88.4	0.006	84.4	0.03	69.3	> 1	20.5	> 1	52.2	0.17384	84.1
OCI-LY19	GCB DLBCL	32910.0	148.0	+ Non-IG	+		2	0.00034	100.5	0.008	102.5	0.10	99.7	> 1	29.9	> 1	35.3	0.05539	94.7
TMD-8	ABC DLBCL	9145.5	17.3				4	0.00006	74.6	0.002	79.3	0.01	70.2	> 1	52.7	0.506	66.1	0.04463	86.4
DB	GCB DLBCL	6.2	531.3	+ Non-IG	+		2	0.00115	94.2	0.013	97.0	0.13	78.4	> 1	17.0	> 1	6.7	0.02991	94.5
NU-DHL-1	GCB DLBCL	285349.3	52.2	+ Non-IG	+		3	0.00008	63.6	0.004	64.8	0.07	62.8	>1	19.4	0.006	46.5	0.02730	57.9
Farage	GCB DLBCL	69514.2	75.8				8	0.00017	76.5	0.003	82.6	0.03	74.5	> 1	26.0	> 1	37.5	0.00392	82.5
KARPAS422	GCB DLBCL	85847.9	54.1				2	0.00002	113.0	0.001	114.5	0.01	96.9	> 1	11.3	> 1	-46.2	0.00117	77.9
SU-DHL-6	GCB DLBCL	3179.6	15.1	+ Non-IG	+		3	0.00029	62.8	0.016	72.9	0.16	72.2	> 1	5.9	3E-05	85.8	0.00003	90.0
JVM-2	MCL	5460.1	37.2				2	0.00002	53.7	0.001	51.0	0.01	53.8	> 1	6.0	4E-05	58.1	0.00003	67.1
OCI-LY7	GCB DLBCL	15557.7	25.8				4	0.0045	57.5	0.104	69.3	3.462	50.5	> 1	11.0	> 1	29.5	0.00002	53.9

Supplemental Table 3

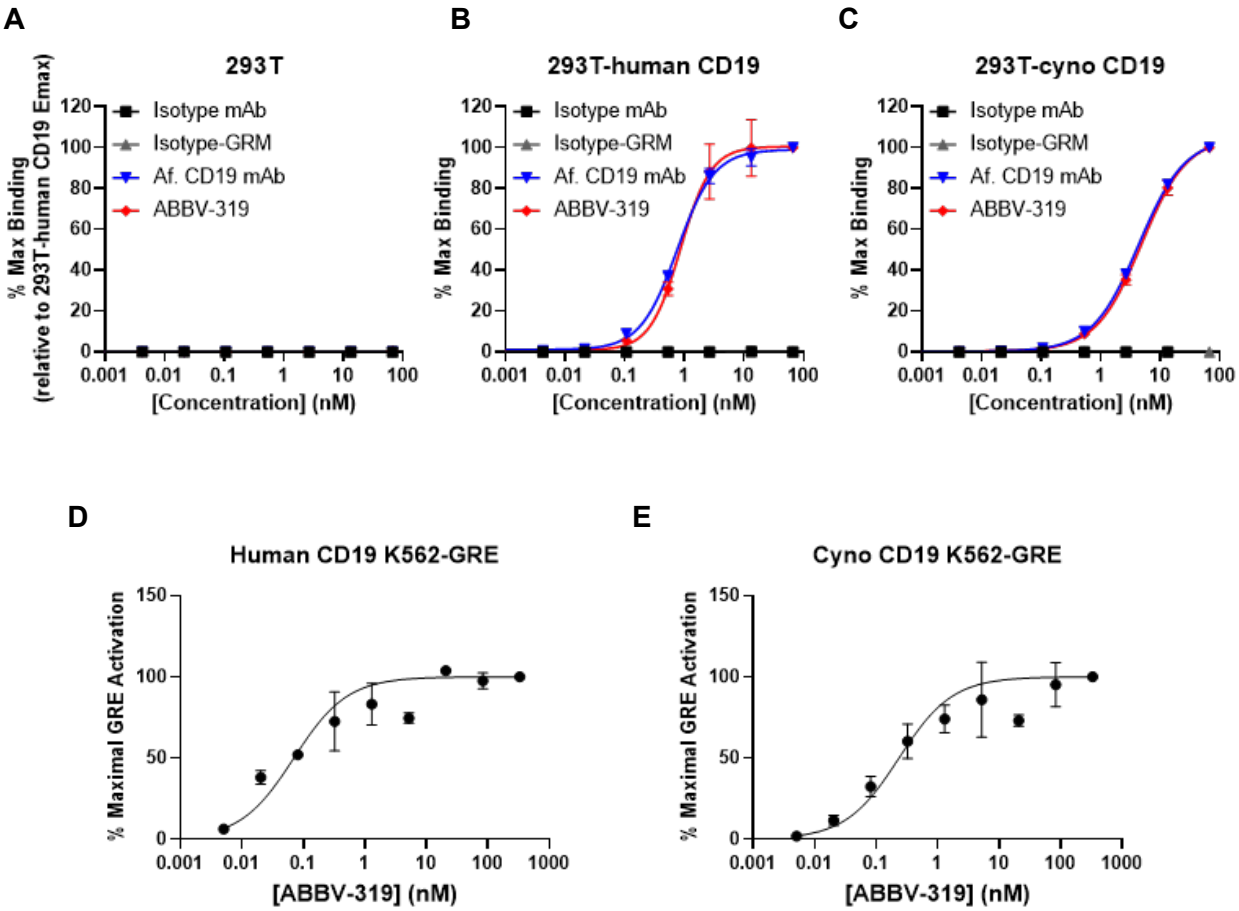
Specificity	Clone	Fluor	Manufacturer	Experiment
CD16	3G8	BUV 496	BD Biosciences	Immunophenotyping
CD19	HIB19	BV 605	BioLegend	Immunophenotyping
CD20	2H7	BV711	BioLegend	Immunophenotyping
CD3	OKT3	APC-Fire 750	BioLegend	Immunophenotyping
CD4	SK3	BUV 805	BD Biosciences	Immunophenotyping
CD45	HI30	BUV 395	BD Biosciences	Immunophenotyping
CD56	HCD56	BV421	BioLegend	Immunophenotyping
CD8a	RPA-T8	AF700	BioLegend	Immunophenotyping
Live/Dead	N/A	Blue	Invitrogen	Immunophenotyping
CD19	HIB19	PE	BD Biosciences	CD19 Quantitation
GR	D8H2	Alexa Fluor 488	Cell Signaling Technologies	GR Expression

Supplemental Table 4

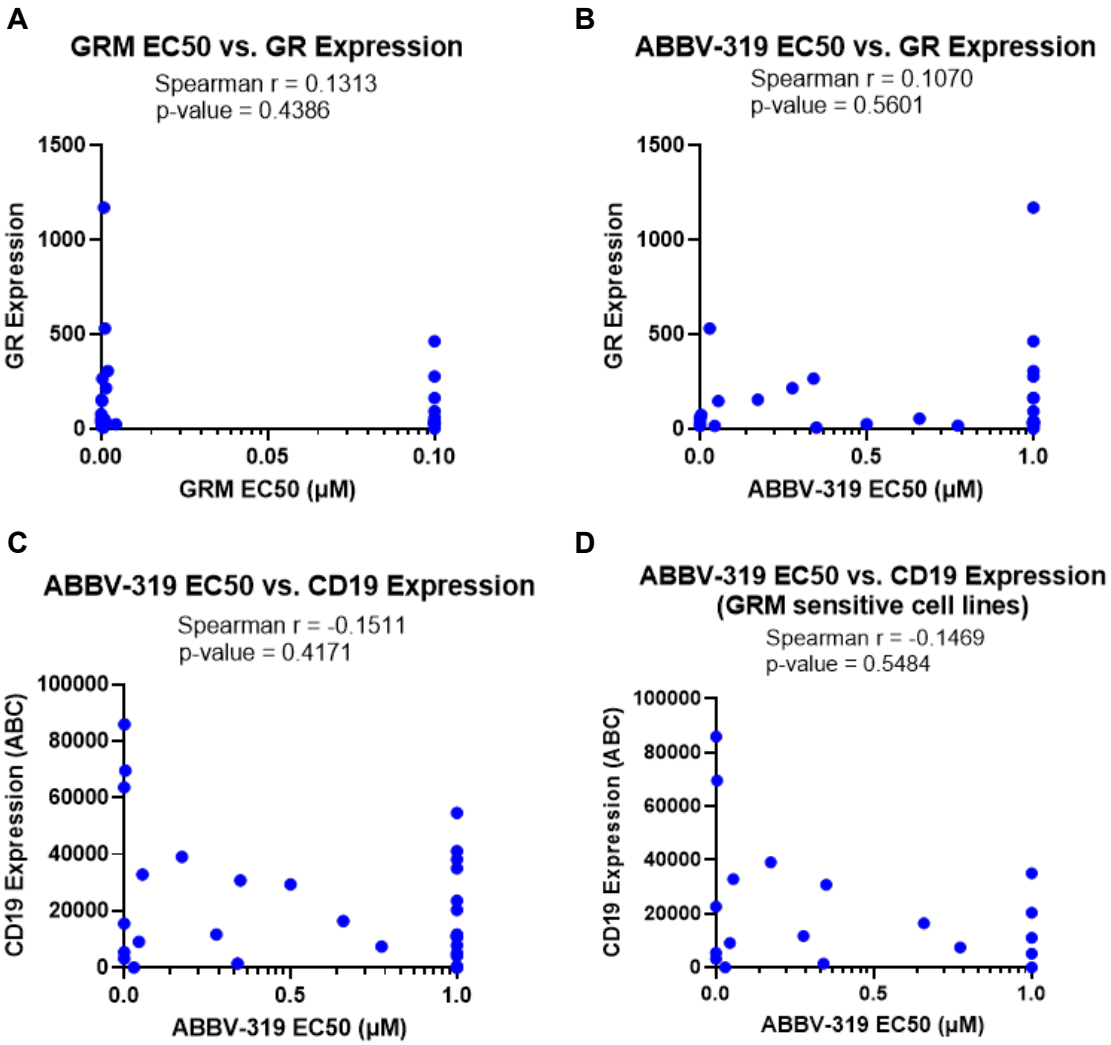
K_D (μM)

	Af. CD19 mAb	ABBV-319
FcγRIIIa F158	0.062	0.052
FcγRIIIa V158	0.047	0.041

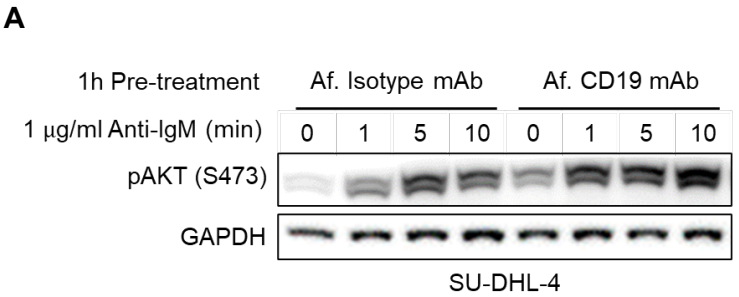
Supplemental Figure 1

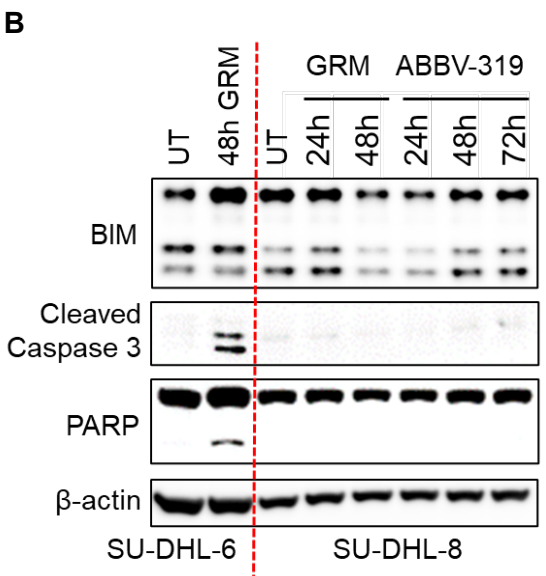


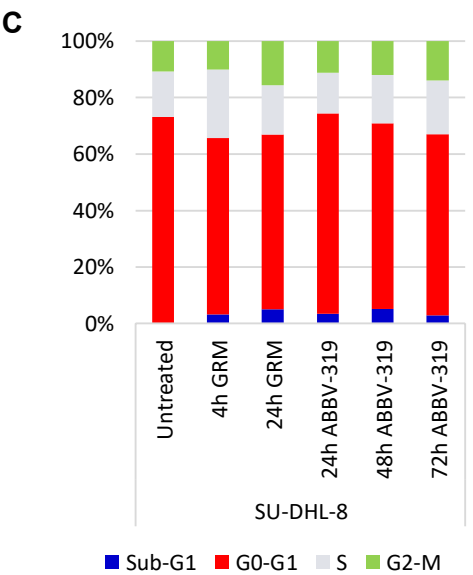
Supplemental Figure 2



Supplemental Figure 3





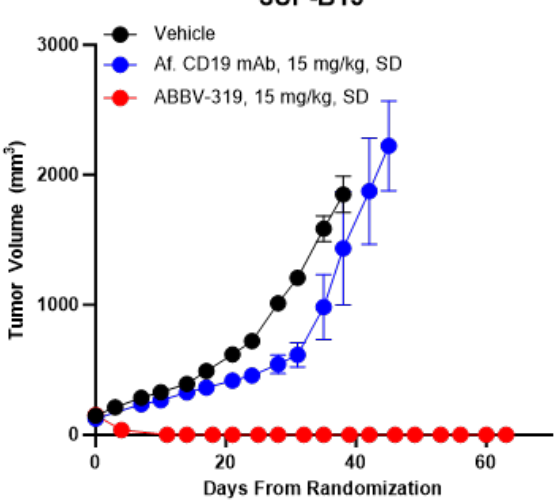


Supplemental Figure 4

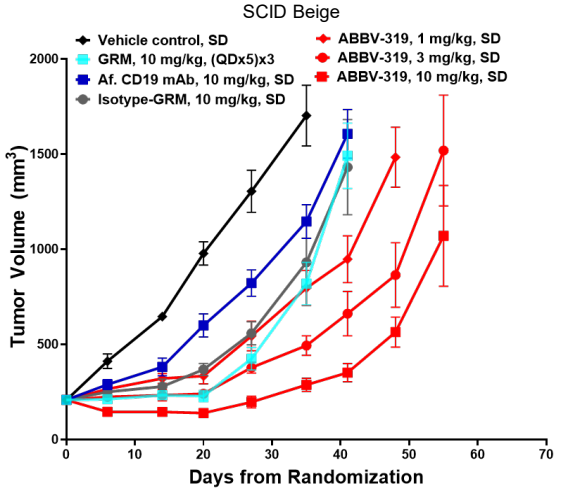
A

Indication	Cell Line	Mouse Strain		In Vivo Efficacy @ 15 mg/kg	
		NSG	CB17 SCID	TGI Max (%)	TGD (days)
ALL	RS4;11	X	X	100	>406
	SUP-B15	X		100	>125
DLBCL	DB		X	100	>139
	DoHH2	X	X	78	79
	OCI-LY19		X	96	510
	KARPASS422		X	97	>212

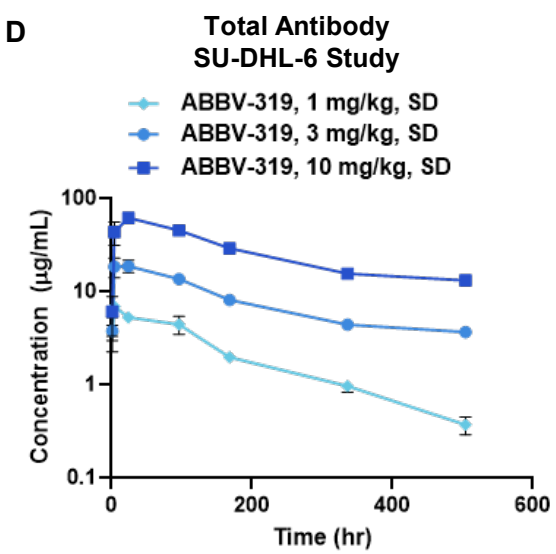
B



C



D



Supplemental Figure 5