Supplementary Figure 1 Combination of GMI-1271 with lenalidomide, carfilzomib or bortezomib overcomes stroma-induced drug resistance in vitro. Survival of H929 cells treated with GMI-1271 (20 µM) and cultured with or without HUVECs +/- lenalidomide (Lenali, 1 µM) (A), with or without MSP-1 +/- carfilzomib (CFZ, 5nM) (B), and with or without HS-5 +/- CFZ (C). Survival of U266 cells treated with GMI-1271 (20 µM) and cultured with or without MSP-1 +/- CFZ (5 nM) (D), with or without HS-5 +/- CFZ (E), and with or without HS-5 +/- BTZ (5 nM) (F). Survival of MM cells was tested at 24 hours using MTT assay. Results are representative of at least three independent experiments and demonstrated as mean ± s.e.m. with statistical significance for p values less than 0.05 calculated using unpaired Student’s t-test (*p<0.05; **p<0.01; ***p<0.001).
Supplementary Figure 2 Combination of GMI-1359 with carfilzomib or bortezomib overcomes stroma-induced drug resistance in vitro. Survival of H929 cells treated with GMI-1359 (20 µM) and cultured with or without MSP-1 +/- carfilzomib (CFZ, 5nM) (A), and with or without HS-5 +/- CFZ (B). Survival of U266 cells treated with GMI-1359 (20 µM) and cultured with or without MSP-1 +/- CFZ (5 nM) (C), with or without HS-5 +/- CFZ (D), and with or without HS-5 +/- BTZ (5 nM) (E). Survival of MM cells was tested at 24 hours using MTT assay. Results are representative of at least three independent experiments and demonstrated as mean ± s.e.m. with statistical significance for p values less than 0.05 calculated using unpaired Student’s t-test (*p<0.05; ***p<0.001).
Supplementary Figure 3 Combination of GMI-1359 with carfilzomib or bortezomib overcomes stroma-induced drug resistance in vitro in the 3D tissue culture model. MM.1S-GFP cells were cultured with and without accessory cells (recapitulating tumor microenvironment, TME) and treated with or without GMI-1359 (25 μM), alone or in combination with carfilzomib (CFZ; 10 nM) (A) or bortezomib (BTZ; 10 nM) (B) in 3DTEBM for 48 hours. Scaffolds were then digested with collagenase and the number of surviving MM.1S-GFP+ cells was analyzed by flow cytometry. Results are representative of at least three independent experiments and demonstrated as mean ± s.e.m. with statistical significance for p values less than 0.05 calculated using unpaired Student’s t-test (*p<0.05).