**Supplemental Figure 1.** Internalization of GA101 (black squares), rituximab (open diamonds), and ofatumumab (open triangles) upon binding to (A) SU-DHL4 cells and (B, C) whole blood derived from two CLL patients. Samples were incubated for 0.5, 2, 4, or 7 h in (A) and for 0.5, 1, 2, 3 and 5 h in (B, C) with Alexa Fluor® 488-labeled GA101, rituximab, or ofatumumab at 37°C, washed and incubated in the presence or absence of anti-Alexa Fluor 488 for 30 min at 4°C. The remaining fluorescence indicates the amount of labeled antibody that is not accessible to the quenching anti-Alexa Fluor 488 antibody and thus corresponds to internalized antibody. The average fluorescence intensity and standard deviations were calculated from duplicates of the experiment with SU-DHL4 cells. Due to low number of primary CLL samples the average fluorescence intensity in B and C correspond to single values.

**Supplemental Figure 2.** Whole-blood B-cell depletion mediated by GA101 (black squares), rituximab (open diamonds), and ofatumumab (open triangles) in lepirudin-treated (A, B) and heat-inactivated (HI) (C) whole-blood samples. GA101 mediated superior B-cell depletion in human whole-blood samples in all experimental conditions (A-C). Heat inactivation of human serum revealed that, in contrast to GA101, ofatumumab and rituximab rely more strongly on complement for efficient B-cell depletion (C). The average B-cell depletion and standard deviations were calculated from the triplicates of each experiment.