Monogenic disorders of the blood system have the potential to be treated by autologous stem cell transplantation of ex vivo genetically modified hematopoietic stem and progenitor cells (HSPCs). Although transient global overexpression of DNA repair factors did not improve the frequency of gene correction in primary HSPCs, localization of factors to the DSB by fusion to the Cas9 protein did alter repair outcomes toward microhomology–mediated end joining (MMEJ) repair, an HDR event. The sgRNA/Cas9 system allows for precise modification of the genome at single nucleotide resolution.