We investigated the feasibility of programmed genome editing in schistosomes. Soluble egg antigen (SEA) and excretory-secretory (ES) products of the egg of *Schistosoma mansoni* contain a glycoprotein T2 family ribonuclease termed omega-1 (ω1). Following release from the egg, ω1 instructs antigen presenting cells to induce naïve $CD4^+$ T cells to mature into T helper 2 (Th2) effectors that, in turn, ultimately drive the immunological phenotype characteristic of schistosomiasis. Schistosome eggs were either transiently exposed to recombinant Cas9 complexed with a synthetic guide RNA (sgRNA) of 20 nt complementary to exon 1 of *ω1* by electroporation, or infected with pseudotyped lentivirus encoding Cas9 and the sgRNA, the latter undertaken to prolong expression of and exposure to sgRNA/Cas9 in the schistosome tissues. Subsequently, the eggs were transduced with single stranded deoxynucleotide bearing 5'- and 3'-homology arms of 50 nt each matching the predicted Cas9-catalyzed double stranded break (DSB) in *ω1* and a central transgene that included six stop codons. Levels of ω1-encoding mRNA were reduced up to 83%, indicative that programmed Cas9 cleavage had mutated the ω1 gene and the DSB in schistosome chromosomes had been resolved by non-homologous end joining (NHEJ) and/or homology direct repair (HDR). Analysis assisted by the CRISPResso pipeline of sequence reads of amplicons spanning the predicted DSB site revealed ~5% of the reads (read depth, 2×10^6) were mutated by insertions, deletions and/or substitutions, with an efficiency for HDR of 0.18% insertion of the donor transgene. Ribonuclease activity of SEA from *ω1*-mutated eggs was diminished markedly and SEA from *ω1*-mutated eggs failed to induce pronounced secretion of Th2 cytokines, IL-4, IL-5 and IL-13 *in vitro*, in comparison to wild-type SEA. To conclude, programmed genome editing was functional and facile in schistosomes, Cas9-catalyzed chromosomal breakage was repaired by NHEJ and/or HDR, and mutation of *ω1* impeded the capacity of schistosome eggs to establish macrophage polarization of inflammation response and polarize $CD4^+$ T cells into Th2 effectors.