A member of the glutathione S-transferase family, Sm28GST has previously demonstrated a good ability to protect rodents against experimental infection with Schistosoma mansoni. In order to evaluate its efficacy in a model closer to man, two different protocols of immunization with recombinant Sm28GST were tested on baboons in a large-scale trial. Three injections in the presence of aluminium hydroxide as adjuvant resulted in a significant 38% reduction in the adult worm burden together with a trend for a lower percentage of inflammatory tissue in the liver. Individual levels of protection, ranging from 0 to 80%, underlined the heterogeneity of the immune response to this purified molecule in outbred primates. On the other hand, two injections of Sm28GST in the presence of aluminium hydroxide and Bordetella pertussis reduced female schistosome fecundity by 33%, with a more pronounced effect (66%) on faecal egg output; there was also a trend, in this protocol, for decrease of the mean granuloma surface in the liver. Individual anti-Sm28GST IgG antibodies were apparently unrelated to levels of immunity, but there was partial evidence that cytophilic IgE might play a role in the immune mechanisms affecting worm viability, but not fecundity. In the mouse model, Sm28GST vaccination resulted in a lower hatching ability of tissue eggs recovered from immunized mice whereas passive transfer of specific anti-Sm28GST T-lymphocytes, one day before infection, significantly reduced the number of eggs in the liver of mice. We propose that different protocols of immunization with a recombinant molecule can impede Schistosoma mansoni worm viability and fecundity, but can also affect miracidium physiology, with important consequences for disease transmission and granuloma-derived pathology.