An HIV vaccine is of high importance for the control of the current pandemic. Outside of screening blood, male circumcision, and drug treatment of mothers and infants at the time of birth, the effectiveness of public health measures has been limited by compliance and cost. Particularly important in the path towards an AIDS vaccine has been the Thai RV144 efficacy trials that showed priming with a poxvirus (ALVAC) and boosting with ALVAC plus gp120 providing partial protection (31% prevention of infection). Analyses for correlates for risk in this trial revealed the association of non-neutralizing antibody (Ab) with protection. Non-neutralizing Abs distinguish themselves from neutralizing Abs by protection being mediated by the Fc regions of bound Ab triggering killing by innate immune responses, such as antibody-dependent cellular cytotoxicity, phagocytosis, and complement-mediated killing; whereas, neutralizing Ab directly block infections through the Fab region of bound Ab blocking infection. The results of RV144 emphasized the importance of polyspecific and polyfunctional non-neutralizing Ab in protection.

GeoVax has developed a clade B vaccine that has undergone Phase 1 and Phase 2a clinical testing in the Americas through the HIV Vaccine Trials Network (HVTN). This vaccine consists of priming with a recombinant DNA vaccine that expresses virus-like particles (VLPs) and then boosting with a recombinant modified vaccinia Ankara (MVA) (an attenuated small pox vaccine) that also expresses VLPs. The VLPs display native trimeric gp160 (DNA) or gp150 (MVA) Env. This vaccine elicits Env-specific Ab in essentially 100%, CD4+ T cells in ~65% and CD8+ T cells in ~20% of vaccinated humans. The Env-specific Ab is biased towards gp41 and is predominantly IgG1 and IgG3 with low serum IgA responses, an isotype profile favorable for protective non-neutralizing Ab. The gp41, but not the gp120 Ab, has excellent longevity, declining by <3-fold in the 6 months post immunization. Studies on regimen reveal delivering the DNA vaccine at 0 and 2 months and the MVA vaccine at 4, 6, and 10 months raises the highest quality Ab responses.

GeoVax is currently developing clade C vaccines from the CHAVI patient 505 who developed broadly neutralizing Ab for the CD4 binding site. This vaccine will allow testing of immunizations with a VLP-displayed Transmitted/Founder Env that can stimulate an unmutated common ancestor for broadly neutralizing Ab for the CD4 binding site (bnAbCD4bs) as well as the use of directed-lineage immunizations with VLP-displayed Envs for bnABCD4bs. The Clade C vaccine has been honed both for design and testing regimen based on the clinical trial results with the GeoVax clade B vaccine.