A successful cancer vaccine will activate the host immune system to induce a balanced T- and B-cell response to tumor-specific antigens that can lead to tumor regression. Effective cancer vaccines will need to overcome several challenges to accomplish this goal, such as to break tolerance to the tumor associated antigens which are mostly self-antigens, induce and maintain high tumor-specific T-cell titers to keep the immune pressure of cytolytic killing of tumor cells as well as to overcome the immune suppressive tumor micro-environment to keep the T cells active at the tumor site. We have applied the lessons learned in the field to the development of a multi-component cancer immunotherapy regimen that has entered clinical testing at the beginning of 2016 for the treatment of patients with prostate cancer. The Vaccine Based Immunotherapy Regimen (VBIR) consists of a chimpanzee adenovirus prime vaccination administered intra-muscularly followed by DNA plasmid boost vaccinations delivered with an electroporation device. With each vaccination low dose of an anti-CTLA4 antibody (tremelimumab) is administered subcutaneously, in close proximity of the vaccine draining lymph nodes. The AdC68 and DNA express the three prostate cancer antigens PSA, PSMA and PSCA. Lastly, to counter the immune suppressive tumor micro-environment, Sutent is added to the regimen to lower myeloid derived suppressor cells at doses that are lower than the approved clinical dose or anti-PD-1 to interfere with the PD-L1/PD-1 signaling pathway.