AVAC
Global Advocacy for HIV Prevention

Selected Guide to Pipeline of Antibodies, Long-Acting ARVs and Vaccines

	What is it?	What could it do?	Key Facts
Antibodies	• Passive immunization is the transfer of pre-made antibodies to a person. Passive immunization using today's pre-made antibodies can involve infusion delivered in a clinic setting over a period of 30 minutes or more. • An alternative approach using vectors and genes that can be turned into "antibody factories" within the body is also under investigation. • Both infusion and gene therapy approaches differ from immunization with vaccines that teach the body how to make its own defenses.	• Laboratory-made broadly neutralizing antibodies (bNAbs) against HIV could provide protection against infection in HIV-negative people. • It might be possible to formulate these bNAbs so that a single dose could provide protection for months at a time. • Testing bNAbs for HIV prevention can also provide proof-of-concept for developing HIV vaccine candidates. • This strategy is being considered for prevention of HIV acquisition in adults and/or breastfeeding infants. • It is also being explored as a treatment modality and perhaps as part of a cure strategy to eliminate viral reservoirs.	• bNAbs are isolated from the blood of people living with HIV. A handful of individuals make these potent immune responses. • The most potent bNAbs come from months of co-evolution with virus during chronic infection. They have unique characteristics. • Some have atypically long regions in the CDR43 loop—a portion of the "arms" of the Y-shaped antibody protein. Others undergo a lengthy process of maturation to become potent against HIV. It will take a long time to create vaccines that elicit such responses.
Long-Acting Injectable (LAI) Antiretrovirals (ARVs)	• Antiretroviral drugs given via injection that persist in the blood for long periods of time. • LAI ARVs need to be dosed every few months. Single-drug LAI PrEP regimens being evaluated utilize injections (one in each buttock) every eight to 12 weeks. • Two-drug LAI treatment regimens being evaluated utilize injections every four or eight weeks.	• In HIV-positive people, LAI ARVs could simplify treatment and change the way ARVs are delivered. • In HIV-negative people, the same ARVs could be long-acting PrEP. This could reduce the burden of adherence and make it easier for some people to take, although issues of regular testing to monitor for HIV infection need to be addressed, as they do for all PrEP strategies (right now PrEP is a daily oral strategy).	• Trials of LAI ARVs start with a lead-in phase where people take oral formulations of the same drugs to establish safety and tolerability in a formulation that can be discontinued. (Injectable ARVs cannot be removed from the body.) • The drugs used as injectables have unique properties that allow them to be formulated into doses suitable for injection. Many other common ARVs can't be used in this way. • The current suite of trials will provide information that could launch expanded trials in 2016/7 designed to test for efficacy and possible licensure for both treatment and prevention purposes.
Preventive Vaccines	• Seeks to teach to the immune system how to protect itself against infection by a pathogen.	• AIDS vaccines have been a key part of the prevention research agenda for nearly three decades. • Existing preventive vaccines for other diseases involve one or a series of immunizations and can provide long-term or even lifelong protection. • Protection isn't always complete and may wane over time. • The one AIDS vaccine strategy to show efficacy to date (in RV144) involved six immunizations and protection waned after one year. • Current research is focused on improving on these results as well as exploring other vaccine candidates entirely.	• There is a robust pipeline of AIDS vaccine work, some of which overlaps with the investigations of passive immunization. • In Southern Africa, work continues on a suite of trials designed to build on the evidence from the RV144 trial. • A range of early-phase trials of other novel candidates to establish the safety and immunogenicity of other novel candidates are getting underway in 2015.

Product Name(s)	Phase of Research	Research Description	HIV Status of Population	Class of Drug	Location
Antibodies*					
3BNC117	Phase I	• Phase I trial in HIV-negative people and people living with HIV looking at safety, tolerability and virologic impact associated with different doses found safety in all groups and sustained viral load reductions at the highest dose. Further treatment and prevention studies are planned.	⊖ ⊕	Broadly neutralizing antibody	Germany, US
AAV vector encoding PG9 antibody	Phase I	• Ongoing Phase I trial is establishing safety and optimal doses of a gene-therapy approach to passive immunization.	⊖	Broadly neutralizing antibody	UK
CAP256-VRC26	Pre-clinical	• Targeting the V1V2 binding site in development for treatment and prevention, currently in preclinical phase.	N/A	Broadly neutralizing antibody	South Africa
Ibalizumab (TMB-355)	Phase I, II	• Ibalizumab has completed Phase I and II trials in HIV-negative individuals and people living with HIV. It is currently available for treatment (as part of combination therapy) via compassionate access programs.	⊖ ⊕	Monoclonal antibody targeting the CD4 binding site	US
PGT121	Pre-clinical	• Targets the V3 region of gp120 and has shown potency in reducing viral load in SIV-infected non-human primates. It is being developed as a possible treatment and/or a component of a cure strategy for people living with HIV.	N/A	Broadly neutralizing antibody	US
VRC01	Phase I	• Targets the gp120 binding site recently being evaluated in a dose escalation study looking at safety, acceptability, PK and PD in people living with HIV. Preliminary results have been reported showing an impact on viral load. • HVTN 104 is Phase I trial evaluating safety and drug levels of this antibody in HIV-negative adults. Concept note for follow-on efficacy trial has been developed. • Phase I saftey trial in infants is also being explored. Planned treatment trials will look at VRC01 + ART in acute infection. Additional trials in HIV-positive and -negative individuals are planned.	⊖ ⊕	Broadly neutralizing antibody	US
Long-Acting Injectable ARVs					
GSK744 (cabotegravir, GSK1265744)	Phase II	• Ongoing ECLAIR trial evaluating safety and tolerability of injections every 12 weeks in HIV-uninfected men in the US. • HPTN 077 evaluating the safety, tolerability and pharmacokinetics in HIV-uninfected men and women.	⊖	Integrase strand transfer inhibitor	Brazil, Malawi, South Africa (HPTN 077), US (HPTN 077 and ECLAIR)
TMC278 (rilpivirine, Edurant)	Phase I, II	• Phase I trial evaluating the safety, acceptability, pharmacokinetics and pharmacodynamics of different dosing regimens underway in men and women in the US. • Phase II placebo-controlled HPTN 076 trial is evaluating safety, acceptability, drug presence in the genital tract of injections at eight week intervals among women in sub-Saharan Africa and the US and is also gathering information on HIV acquisition.	⊖	Nonnucleoside reverse transcriptase inhibitor	South Africa, US, Zimbabwe
TMC278/GSK744	Phase IIb	• A two-drug combination being tested as a "maintenance" regimen in people living with HIV who have achieved virologic suppression on triple-combination oral ARVs.	⊕	Nonnucleoside reverse transcriptase inhibitor plus integrase strand transfer inhibitor	Canada, France, Germany, Spain, US
Preventive Vaccines*					
Ad26/MVA/gp140	Phase I/II	• Trial testing safety and immunogenicity of various regimens containing Ad26 vector (a cold-causing virus, altered to not cause illness) and a "mosaic" immunogen, designed to induce immunity against a range of HIV subtypes.	⊖	Adenovirus 26/ Modified Vaccinia Ankara Mosaic/ glycoprotein 140	South Africa, Thailand, US
ALVAC/AIDSVAX	Phase III follow-up and Phase I	• RV305 is taking place among participants from original RV144 trial to assess impact of additional boosts. • RV306 is testing the boosted regimen among new participants.	⊖	Pox-protein	Thailand
ALVAC/gp120/ MF59 adjuvant Clade C	Phase I/II	• HVTN 100 is testing an RV144-like regimen that has been altered with goal of optimizing for southern Africa. • First trial in the "development track" of post-RV144 trials sponsored by the Pox-Protein Public-Private Partnership (P5).	⊖	Pox-protein	South Africa
ALVAC, DNA, Protein, MF59, AS01B adjuvant (various combinations)	Phase I/II	• Suite of trials in the P5 "research track" will evaluate various vaccine combinations to identify correlates of immunity that could improve future regimens.	⊖	Pox-protein	Malawi, Mozambique, South Africa, Switzerland, Tanzania, US, Zambia, Zimbabwe

* The list of clinical and preclinical trials below is not exhaustive. For details on full range of products in ongoing and completed trials visit *avac.org/pxrd*.