

Pipeline Report » 2026

HIV Vaccines and Passive Immunization

The HIV Vaccines and Passive Immunization Pipeline Report 2026

By Richard Jefferys

The development of an effective immunization strategy against HIV remains essential for ending the epidemic. The options for HIV prevention with pre-exposure prophylaxis (PrEP) have greatly expanded in recent years, yet the potential for very broad implementation is curtailed by a number of factors, including accessibility, antiretroviral drug tolerance, potential for drug interactions, adherence, and recognition of a risk of acquisition.

These limitations have only been exacerbated by the active hostility of ideologues in the current U.S. administration (and a number of other governments) toward supporting PrEP provision for populations most likely to be exposed to HIV. An ideally safe and effective HIV vaccine would provide long-term protection and could be administered without an assessment of the possibility of encountering the virus.

An HIV vaccine is yet to be developed because the virus presents multiple difficult obstacles to effective immunization. Among them is that HIV infects and disrupts CD4 T cells, which typically coordinate the immune response to pathogens. A vaccine therefore needs to induce immune responses that won't be directly undermined by the virus infecting the CD4 T cells that should be leading the charge. The integration of HIV's genetic code into the genome of infected CD4 T cells is another major hurdle; only two people ([Loreen Willenberg](#) and [the Esperanza Patient](#)) have shown evidence of immune-mediated clearance of all viable HIV from their bodies without other interventions, and this process occurred over decades.

Despite these obstacles, in recent years HIV vaccine research has provided reason to hope that inducing high levels of effective ("broadly neutralizing") antibody responses against the virus can be protective and prevent the establishment of persistent infection. But challenges remain: HIV has evolved to be highly resistant to antibody-mediated neutralization, and the types of antibodies that can strongly block a wide range of global virus variants are rare and will likely require a novel multistep vaccine approach to guide their development.

Encouragingly, the past year has seen reports of significant progress toward solving the conundrum of inducing broadly neutralizing antibodies (bNAbs) in both macaque monkey models and human clinical trials. The science can be difficult to follow because it doesn't yet involve typical vaccine candidates on a pathway toward efficacy testing and regulatory approval but rather a variety of proteins, adjuvants (immune-response enhancing substances), and delivery methods aimed at establishing a blueprint for a vaccine regimen that could be advanced into efficacy trials.

As recently outlined in a [technical summary](#) by researchers Barton Haynes, Chen-Hao Yeha, and Lindsey Baden, this work has been dubbed "discovery medicine" and seeks to guide B cells to produce bNAbs against a variety of potentially vulnerable targets on HIV's outer envelope. These include the membrane proximal external region, CD4 binding site, and two variable loops (named V2 and V3). A somewhat bewildering array of codenames are attached to the proteins being tested, representing carefully selected constructs that aim to raise the number of B cells with a profile amenable to further stimulation toward

bNAb production and others designed to provide this additional stimulus. A variety of more complex and intact mimics of the three-pronged structure of the HIV envelope — known as trimers — are also under evaluation for their capacity to coax B cells along the pathway that leads to bNAb generation.

This approach is called germline targeting, which means targeting and increasing the number of B cells with a baseline genetic code (germline) known to represent a starting point for bNAb production. These B cells can then be further stimulated by additional booster immunizations to undergo somatic hypermutation, during which the baseline genetic code gets progressively revised to generate antibodies with increasing neutralization capacity. Researchers call the sequence of specially designed booster immunizations “shepherding” and “polishing” the B-cell response.

An [open access commentary](#) by Rowena Bull and Deborah Burnett describes the results of three studies published in 2026 that tested this strategy in macaques. Importantly, evidence of bNAb generation was documented in a substantial proportion of animals, which the authors laud as “a turning point in HIV vaccinology,” although they note that work remains to translate the advances into a vaccine candidate. The commentary concludes:

“Together, these studies highlight potential avenues that could be expanded beyond just HIV to develop germline-targeting vaccine approaches for other rapidly evolving RNA viruses, such as influenza and hepatitis C.”

The majority of the clinical trials listed in the pipeline table below are testing various components of germline-targeting strategies, although there are some exceptions, such as the Worcester Vaccine (focused more on antibody responses that can bind to HIV but aren’t necessarily neutralizing) and two attenuated viral vectors (gorilla adenovirus and human cytomegalovirus) designed to induce anti-HIV T-cell responses that may help supplement antibody-based vaccines.

Notably, three of the trials are enrolling people with HIV on antiretroviral therapy (ART) rather than HIV-negative participants. In two cases, the study protocols include analytical treatment interruptions (ATIs) to assess how antibody responses induced by the vaccine constructs are modulated when B cells are exposed to a rebound in HIV viral load. A third trial in Switzerland, where ART will be maintained throughout, will assess the effects of immunization with an HIV envelope trimer protein in people with HIV.

Researchers continue to investigate whether direct delivery of bNAbs — passive immunization — can be a viable approach to immune-based HIV prevention (essentially PrEP with bNAbs instead of antiretroviral drugs).

Preliminary results from CAPRISA 012C in South Africa, one of the ongoing dual bNAb passive immunization studies in the table, were [presented at the AIDS 2026 conference](#) by principal investigator Sharana Mohamed (who also subsequently shared the information on an [AVAC community webinar](#)). Disappointingly, the bNAbs were ineffective at preventing HIV acquisition, but the data generated will help inform the field.

The two bNAbs were CAP256V2LS and VRC07-523LS, which can strongly suppress multiple HIV variants in a laboratory dish. CAP256V2LS specifically targets HIV subtype C, which is most prevalent in the region. The trial recruited 1,023 young women who were randomly assigned to receive either the bNAbs or a placebo (a dummy shot) by subcutaneous injection every six months. To ensure the study was ethical, PrEP was offered to all participants; usage was low at baseline but nearly 40% of participants in each of the two groups initiated Truvada PrEP during the trial. Both bNAbs were safe, with the main side effect being transient injection site reactions.

Receipt of the bNAbs didn't significantly reduce the risk of HIV acquisition in the study. There were 22 cases among the 512 participants in the bNAbs group and 17 out of 511 in the placebo group, making the HIV incidence statistically indistinguishable between the study arms. There was some limited evidence of protection against HIV variants with greater susceptibility to inhibition by the bNAbs: few participants acquired viruses susceptible to one of the two bNAbs, and no participants acquired HIV susceptible to both.

Concerningly, levels of resistance to the bNAbs among locally circulating viral variants appeared to be high. Of the 17 participants in the placebo arm who acquired HIV, 12 (71 %) showed viral resistance to CAP256V2LS, 10 (59%) resistance to VRC07-523LS, and seven (41%) resistance to both bNAbs. These results demonstrate the vital importance of understanding the bNAb resistance profiles of contemporary HIV variants in any population where a passive immunization regimen may be tested for protective efficacy.

An unexpected finding from a preparatory study is that CAP256V2LS appears to lose neutralizing activity a few weeks after administration even when antibody levels are maintained (a phenomena that has not been documented with VRC07-523LS or other bNAbs). A [published preprint](#) notes that there are a number of possible mechanisms by which this could occur, and ongoing studies are now attempting to hone in on the culprit.

Two new trials have been added to the passive immunization table below, both evaluating bNAb combinations including ePGT121v1-LS, developed by the nonprofit [IAVI](#):

- In a [collaboration](#) with the HIV Vaccine Trials Network (HVTN) and HIV Prevention Trials Network (HPTN), ePGT121v1-LS will be tested with PGDM1400LS and VRC07-523LS in HIV-negative adults. The phase I protocol will assess a range of doses administered intravenously or subcutaneously.
- A phase I trial sponsored by the South African Medical Research Council in collaboration with Ospedale San Raffaele in Italy will initially administer ePGT121v1-LS with HIV-negative adults, either alone or in combination VRC07-523LS. If the adult safety results are supportive, the study will progress to testing the bNAbs in infants. The research is part of a collaborative program called the [PedMab Consortium](#).

The ultimate aim of these two studies is to develop a passive immunization regimen to prevent HIV transmission to infants during the postnatal period.

As noted in last year's Pipeline Report, the current political situation in the United States represents the most significant threat to the development of an effective HIV vaccine or passive immunization regimen. The majority of the clinical research listed in this report is supported by the U.S. National Institutes of Health (NIH), whose leadership is now pursuing "America First" policies. NIH funding for the Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery – a collaboration responsible for much of the progress toward inducing bNAbs with vaccines – was [terminated in 2025](#), despite an initial forecast of a modified renewal.

Translation of scientific advances into the clinic falls to the NIH-supported HIV clinical trial networks including HVTN, HPTN, the International Maternal, Pediatric, Adolescent AIDS Clinical Trials ([IMPAACT](#)) Network, and Advancing Clinical Therapeutics Globally ([ACTG](#)). The current grant cycle for these networks ends November 30, 2027, and notices to apply for renewed funding for another seven years were forecast to be issued on August 25, 2026, after passing every level of review within NIH. These notices are now stalled at the Department of Health and Human Services and, as [recently reported by the New York Times](#), may be under threat.

Advocates working under the umbrella of the [Save HIV Funding Campaign](#) are writing to Congress to flag the importance of the networks and their contributions not only to HIV but to multiple conditions including tuberculosis, hepatitis, and emerging infectious diseases.

The threats to HIV research are part of a broader campaign by the Executive Branch and their Congressional allies to assail and undermine science. TAG is among many groups working with larger collaborative efforts such as [Stand Up For Science](#) and [Defend Public Health](#) to push back. We urge everyone who values scientific research and the continued development of interventions to treat and prevent all health conditions to join and support these campaigns.

Table: HIV Vaccines and Passive Immunization Pipeline 2026 (Active Clinical Trials)

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/Sponsor	Status
HIV VACCINES				
Polyvalent env (A,B,C,A/E)/gag (C) DNA prime gp120 (A,B,C,A/E) protein HIV-1 vaccines boost (PDPHV) with either Alhydrogel or GLA-SE		NCT07675629	Worcester HIV Vaccine	Phase II
- Moodie Z, Li SS, Giorgi EE, et al. A polyvalent DNA prime with matched polyvalent protein/GLA-SE boost regimen elicited the most robust and broad IgG and IgG3 V1V2 binding antibody and CD4+ T cell responses among 13 HIV vaccine trials. <i>Emerg Microbes Infect.</i> 2025 Dec;14(1):2485317 - Frank I, Li SS, Grunenberg N, et al. Safety and immunogenicity of a polyvalent DNA-protein HIV vaccine with matched Env immunogens delivered as a prime-boost regimen or coadministered in HIV-uninfected adults in the USA (HVTN 124): a phase 1, placebo-controlled, double-blind randomised contr. <i>Lancet HIV.</i> 2024 May;11(5):e285-e299.				
Ad4-Env145NFL Ad4-Env150KN VRC-HIVRGP096-00-VP (Trimer 4571) /alum	Replication-competent Ad4 HIV vaccines encoding Env proteins + native-like HIV-1 Env trimer with alum adjuvant	NCT03878121	NIAID	Phase I
Houser KV, Gaudinski MR, Happe M, et al. Safety and immunogenicity of an HIV-1 prefusion-stabilized envelope trimer (Trimer 4571) vaccine in healthy adults: a first-in-human open-label, randomized, dose-escalation, phase 1 clinical trial. <i>EClinicalMedicine.</i> 2022 Jun 1;48:101477.				
BG505 MD39.3 BG505 MD39.3 gp151 BG505 MD39.3 gp151 CD4KO HIV trimer mRNA vaccines	mRNA vaccines encoding one of three HIV trimer proteins: BG505 MD39.3, BG505 MD39.3 gp151, or BG505 MD39.3 gp151 CD4KO	NCT05217641 (HVTN 302)	NIAID	Phase I
- Parks KR, Moodie Z, Allen MA, et al. Vaccination with mRNA-encoded membrane-anchored HIV envelope trimers elicited tier 2 neutralizing antibodies in a phase 1 clinical trial. <i>Sci Transl Med.</i> 2025 Jul 30;17(809):eady6831. - National Institutes of Health. NIH launches clinical trial of three mRNA HIV vaccines. [Press Release]. 2022 Mar 14. - Steichen JM, Kulp DW, Tokatlian T, et al. HIV vaccine design to target germline precursors of glycan-dependent broadly neutralizing antibodies. <i>Immunity.</i> 2016 Sep 20;45(3):483-496.				

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/Sponsor	Status
V3G CH848 Pr-NP1 + V3G CH848 mRNA-Tr2 lipid nanoparticle with 3M-052 AF + alum adjuvant	Ferritin nanoparticles expressing eight copies of an Env trimer + mRNA lipid nanoparticle encoding a soluble Env trimer + TLR 7/8 agonist 3M-052 AF + alum adjuvants	NCT05903339 (HVTN 307)	NIAID	Phase I
Haynes BF, Wiehe K, Alam SM, Weissman D, Saunders KO. Progress with induction of HIV broadly neutralizing antibodies in the Duke Consortia for HIV/AIDS Vaccine Development. <i>Curr Opin HIV AIDS</i>. 2023 Nov 1;18(6):300-308.				
Ad26.Mos4.HIV + CH505 TF chTrimer	Adenovirus vector + stabilized CH505 TF chTrimer protein	NCT06205056 (RV 591)	U.S. Army Medical Research and Development Command	Phase I
16055 NFL Delta Gly4 Env Trimer + Trimer 4571 + 3M-052-AF + alum adjuvant + Ad4-Env145NFL viral particles	Env protein trimers + 3M-052-AF + alum adjuvant + replication-competent Ad4 HIV vaccines encoding Env protein	NCT06332339 (HVTN 313)	NIAID	Phase I
CH505M5 N197D mRNA-gp160 + CH505 TF mRNA-gp160	mRNA vaccines encoding Env protein trimers	NCT06557785 (HVTN 312)	NIAID	Phase I
426c.Mod.Core-C4b vaccine + 3M-052-AF + Alum in infants	Engineered protein priming immunogens designed to sequentially activate B-cell precursors as steps toward induction of bNAbs + Alum adjuvant	NCT06613789 (HVTN 316)	NIAID	Phase I
Hahn W, Parks KR, De Rosa S, et al. Vaccination with a novel fractional escalating dose strategy improves early humoral responses with a novel germline targeting HIV vaccine (426.mod.core-C4b): preliminary results from HVTN 301 (Abstract OA1204). Paper presented at: R4P 2024; 2024 October 6-10; Lima, Peru.				
Gorilla adenovirus vectored networked epitopes vaccine	Gorilla adenovirus vector encoding networked HIV T-cell epitopes	NCT06617091 (IAVI C114)	IAVI	Phase I
CD40.HIVRI.Env (VRIPRO) + Hiltonol adjuvant	HIV Env protein + Poly-ICLC adjuvant	NCT06665646 (HVTN 318)	NIAID	Phase I
Levy Y, Moog C, Wiedemann A, et al. Safety and immunogenicity of CD40.HIVRI.Env, a dendritic cell-based HIV vaccine, in healthy HIV-uninfected adults: a first-in-human randomized, placebo-controlled, dose-escalation study (ANRS VRI06). <i>EClinicalMedicine</i>. 2024 Oct 2;77:102845.				
eOD-GT8 60mer, core-g28v2 60mer, N332-GT5 gp151	mRNA vaccines encoding engineered priming immunogens designed to sequentially activate B-cell precursors as steps toward induction of bNAbs	NCT06694753 (HVTN 317)	NIAID	Phase I
Leggat DJ, Cohen KW, Willis JR, et al. Vaccination induces HIV broadly neutralizing antibody precursors in humans. <i>Science</i>. 2022 Dec 2;378(6623):eadd6502				

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/Sponsor	Status
426c.Mod.Core-C4b + HxB2. WT.Core-C4b with 3M-052 AF + Alum adjuvant	Engineered protein priming immunogens designed to sequentially activate B-cell precursors as steps toward induction of bNAbs + Alum adjuvant	NCT06796686 (HVTN 320)	NIAID	Phase I
Hahn W, Parks KR, De Rosa S, et al. Vaccination with a novel fractional escalating dose strategy improves early humoral responses with a novel germline targeting HIV vaccine (426.mod.core-C4b): preliminary results from HVTN 301 (Abstract OA1204). Paper presented at: R4P 2024; 2024 October 6-10; Lima, Peru.				
UVAX-1107 + UVAX-1197 with 3M-052-AF + Alum adjuvant	Glycan-trimmed HIV-1 nanoparticle + homologous or wild-type HIV-1 nanoparticle vaccines	NCT06905275 (HVTN 319) (paused to accrual)	NIAID	Phase I
- Garbes P, Chang C, Wright H, et al. P-325. An Innovative Approach For An HIV-1 Prophylactic Vaccine – Results From A Phase I Clinical Trial. Open Forum Infect Dis. 2026 Jan 11;13(Suppl 1):ofaf695.544. - Tatoud R, Brander C, Hwang C, et al. Biotech's role in advancing HIV vaccine development. Emerg Microbes Infect. 2024 Dec;13(1):2384460. - Zhang YN, Paynter J, Antanasijevic A, et al. Single-component multilayered self-assembling protein nanoparticles presenting glycan-trimmed uncleaved prefusion optimized envelope trimmers as HIV-1 vaccine candidates. Nat Commun. 2023 Apr 8;14(1):1985.				
DV700P-RNA + DV701B1.1-RNA	mRNA-encoded HIV Env V3 region-directed immunogens	NCT06919016 (HVTN 321)	NIAID	Phase I
DV201P-RNA + DV202B1-RNA	HIV Env V2 apex-directed immunogens	NCT07390474 (HVTN 322)	NIAID	Phase I
426c.Mod.Core-C4b + 3M-052-AF + Alum adjuvant	Engineered protein priming immunogens designed to sequentially activate B-cell precursors as steps toward induction of bNAbs + Alum adjuvant	NCT06006546 (HVTN 807)	NIAID	Phase I
- ATI study that enrolled people with HIV on ART. - Stephenson K. HVTN 807 Results. Paper presented at: HVTN Full Group Meeting 2026; 2026 May 6-8; Washington, DC.				
DV700P-RNA + DV701B1.1-RNA	mRNA-encoded HIV Env V3 region-directed immunogens	NCT07569029 (HVTN 808)	NIAID	Phase I
ATI study enrolling people with HIV on ART.				

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/Sponsor	Status
CH505 nanoparticles + mRNA boosts	CH505 protein nanoparticle vaccines (DV901-NP) with investigational adjuvant ACU-026-001-1 + either DV902-NP or CH505 mRNA vaccine boosters	NCT07757802 (HVTN 324)	NIAID	Phase I
BG505 SOSIP.v4.1-GT1.1 + 3M-052-AF + Alum adjuvant	Germline-targeting envelope trimer protein + Alum adjuvant	NCT07769983	University of Zurich	Phase I
- Study enrolling people with HIV on ART from the Swiss HIV Cohort Study, the protocol doesn't involve an ATI. - Trkola A, Moore PL. Vaccinating people living with HIV: a fast track to preventive and therapeutic HIV vaccines. Lancet Infect Dis. 2024 Apr;24(4):e252-e255. - Kouyos RD, Rusert P, Kadelka C, et al. Tracing HIV-1 strains that imprint broadly neutralizing antibody responses. Nature. 2018 Sep;561(7723):406-410.				
VIR-1388	CMV vector	NCT07801456 (HVTN 146)	NIAID	Phase I
PASSIVE IMMUNIZATION				
VRC07-523LS, PGT121.414.LS, PGDM1400LS	Long-acting (LA) bNAbs administered intravenously	NCT06812494 (HVTN 206/HPTN 114)	NIAID	Phase II
- Huang Y, Zhang L, Gelderblom H, et al. Fixed dosing versus weight-based dosing of HIV-1 prophylactic monoclonal antibodies in adults: a post-hoc, cross-protocol pharmacokinetics modelling study. EBioMedicine. 2025 Jul;117:105804. - Edupuganti S, Hurt CB, Stephenson KE, et al. Safety, tolerability, pharmacokinetics, and neutralisation activities of the anti-HIV-1 monoclonal antibody PGT121.414.LS administered alone and in combination with VRC07-523LS in adults without HIV in the USA (HVTN 136/HPTN 092): a first-in-human, open-l. Lancet HIV. 2025 Jan;12(1):e13-e25.				
CAP256V2LS VRC07-523LS	LA bNAbs administered subcutaneously ± recombinant human hyaluronidase PH20 (rHuPH20)	PACTR202112683307570 (CAPRISA 012C)	CAPRISA	Phase II
- Mahomed S, Osman F, Harkoo I, et al. Safety and preliminary efficacy of 6-monthly subcutaneous CAP256V2LS plus VRC07-523LS for HIV prevention in African women: results of the CAPRISA 012C phase 2 randomised controlled trial. Paper presented at: AIDS 2026; 2026 July 26-31; Rio, Brazil. - Mahomed S, Garrett N, Potloane D, et al. Extended safety and tolerability of subcutaneous CAP256V2LS and VRC07-523LS in HIV-negative women: study protocol for the randomised, placebo-controlled double-blinded, phase 2 CAPRISA 012C trial. BMJ Open. 2023 Aug 28;13(8):e076843.				

Agent	Class/Type	Trial Registry Identifier(s)	Manufacturer/Sponsor	Status
CAP256V2LS VRC07-523LS PGT121	LA and non-LA bNAbs administered subcutaneously ± recombinant human hyaluronidase PH20 (rHuPH20)	PACTR202003767867253 (CAPRISA 012B)	CAPRISA	Phase I
■ Sobia P, Mahomed S, Sivo A, et al. Circulating immunoglobulins and transient lymphocytopenia in a sub-study of CAPRISA 012B, testing HIV monoclonal antibodies in a phase 1 trial. Sci Rep. 2024 Jun 12;14(1):13499. ■ Mahomed S, Garrett N, Capparelli EV, et al. Safety and pharmacokinetics of escalating doses of neutralising monoclonal antibody CAP256V2LS administered with and without VRC07-523LS in HIV-negative women in South Africa (CAPRISA 012B): a phase 1, dose-escalation, randomised controlled trial. Lancet HIV. 2023 Apr;10(4):e230–e243. ■ Mahomed S, Garrett N, Karim QA, et al. Assessing the safety and pharmacokinetics of the anti-HIV monoclonal antibody CAP256V2LS alone and in combination with VRC07-523LS and PGT121 in South African women: study protocol for the first-in-human CAPRISA 012B phase I clinical trial. BMJ Open. 2020 Nov 26;10(11):e042247.				
PGT121.414.LS +/- VRC07-523LS in infants	LA bNAbs administered subcutaneously	NCT06517693 (IMPAACT 2037)	NIAID	Phase I
■ Cunningham CK, McFarland EJ, Muresan P, et al. Safety, tolerability, and pharmacokinetics of long-acting broadly neutralizing HIV-1 monoclonal antibody VRC07-523LS in newborn infants exposed to HIV-1. J Pediatric Infect Dis Soc. 2025 Feb 6;14(2):piaf002.				
ePGT121v1-LS PGDM1400LS VRC07-523LS	LA bNAbs administered intravenously or subcutaneously	NCT07390955 (HVTN 141/HPTN 105)	NIAID	Phase I
ePGT121v1-LS +/- VRC07-523LS	LA bNAbs administered subcutaneously or intramuscularly	PACTR202603555334830	South African Medical Research Council	Phase I

Shaded entries represent additions since the 2025 Pipeline Report.

Ad4: adenovirus serotype 4

ART: antiretroviral therapy

ATI: analytical treatment interruption

bNAbs: broadly neutralizing antibody

CMV: Cytomegalovirus

GLA-SE: glucopyranosyl lipid adjuvant formulated in a stable emulsion

HPTN: HIV Prevention Trials Network

HVTN: HIV Vaccine Trials Network

IAVI: International AIDS Vaccine Initiative

IMPAACT: International Maternal, Pediatric, Adolescent AIDS Clinical Trials Network

LA: long-acting

mRNA: messenger RNA

NIAID: U.S. National Institute of Allergy and Infectious Diseases

NIH: U.S. National Institutes of Health

PrEP: pre-exposure prophylaxis

R4P: HIV Research for Prevention Conference

TLR: toll-like receptor

VRC: The Dale and Betty Bumpers Vaccine Research Center