Beyond Antiretrovirals: The Next Frontier in HIV Therapeutics

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Received: Sep 01, 2025, Manuscript No. JHAR-25-169616; **Editor assigned:** Sep 03, 2025, PreQC No. JHAR-23-169616 (PQ); **Reviewed:** Sep 18, 2025, QC No. JHAR-23-169616; **Revised:** Sep 23, 2025, Manuscript No. JHAR-23-169616 (R); **Published:** Sep 30, 2025, DOI: 10.35248/JHAR.25.7(2).001

Abstract

For over three decades, antiretroviral therapy (ART) has been the cornerstone of HIV treatment, transforming a once-lethal diagnosis into a manageable chronic condition. Yet, as science advances and the needs of people living with HIV evolve, researchers and clinicians are looking beyond viral suppression toward a more holistic and innovative therapeutic landscape. The next frontier in HIV therapeutics encompasses long-acting formulations, immune-based therapies, gene editing, and precision medicine—all aimed at improving quality of life, reducing stigma, and ultimately achieving a cure.

Keywords: HIV cure strategies • Latent reservoir eradication • Immunotherapy • Therapeutic vaccines

Introduction

While ART has drastically reduced AIDS-related mortality, it is not without limitations. Daily adherence remains a challenge for many, particularly in marginalized populations. Long-term use of ART can lead to metabolic complications, chronic inflammation, and accelerated aging—even when viral loads are undetectable. Telemedicine and mobile health platforms are revolutionizing HIV care delivery. These tools facilitate remote monitoring, virtual consultations, and digital adherence support, making care more accessible—especially in rural or underserved areas. Integration of digital health into HIV therapeutics enhances patient engagement and continuity of care. Moreover, ART does not eliminate latent reservoirs of HIV, which remain a major barrier to a cure [1].

One of the most promising developments is long-acting injectable ART. Immune modulation is another emerging strategy. Broadly neutralizing antibodies (bNAbs) target multiple strains of HIV and can suppress viral replication without daily medication. These antibodies are being tested both as treatment and prevention tools. Additionally, therapeutic vaccines aim to train the immune system to recognize and eliminate HIV-infected cells, potentially reducing the need for lifelong ART. Drugs like cabotegravir and rilpivirine, administered monthly or bimonthly, offer an alternative to daily pills. These formulations improve adherence, reduce stigma, and are especially beneficial for individuals with unstable housing or mental health challenges. Clinical trials have shown that long-acting injectables can maintain viral suppression effectively [2].

Gene editing technologies like CRISPR-Cas9 offer a radical approach: directly excising HIV DNA from infected cells. Early studies have demonstrated the feasibility of removing proviral DNA from human cells in vitro. Therapeutic advances must be matched by structural reforms. Equitable access to cutting-edge treatments requires policy changes that integrate HIV care into primary health systems, reduce stigma, and address social determinants of health. Community-based models and peer-led interventions are also vital for improving uptake and retention. While clinical application is still in its infancy, gene editing holds promise for a functional cure—where the virus is controlled without ongoing treatment [3].

HIV's ability to hide in latent reservoirs is a major obstacle to eradication. Latency-reversing agents (LRAs) aim to "shock" the virus out of hiding, allowing the immune system or therapeutic agents to "kill" the exposed cells. Though results have been mixed, combining LRAs with immune therapies may enhance efficacy [4].

Advances in genomics, proteomics, and metabolomics are enabling personalized HIV care. By analyzing individual genetic and molecular profiles, clinicians can tailor ART regimens to minimize side effects and maximize efficacy. People living with HIV often face comorbid conditions such as cardiovascular disease, neurocognitive decline, and osteoporosis. Future therapeutics must integrate HIV care with broader health management. This includes screening for age-related conditions and developing ART regimens that minimize systemic toxicity. Machine learning models are also being developed to predict treatment outcomes and guide clinical decisions [5].

Conclusion

The ultimate goal remains a cure—either sterilizing (eliminating all virus) or functional (controlling virus without ART). While no cure exists yet, the convergence of gene editing, immune therapies, and precision medicine is bringing this vision closer to reality. Continued investment in research, community engagement, and global collaboration will be essential.

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Cite this article: Amany Awad. "Beyond Antiretrovirals: The Next Frontier in HIV Therapeutics". J HIV AIDS Res, 2025, 7(2), 01-02.