

# “Towards an **HIV** Cure”

Scientific research has led to remarkable discoveries since HIV was first identified thirty years ago. Today, individuals living with HIV can expect to live a relatively normal lifespan provided they are both diagnosed and treated early enough and they comply to life-long antiretroviral drug regimens.

However, combination therapy – even when taken for decades – is not curative, as HIV persists despite even the best treatment.

# Why do we need to cure HIV?

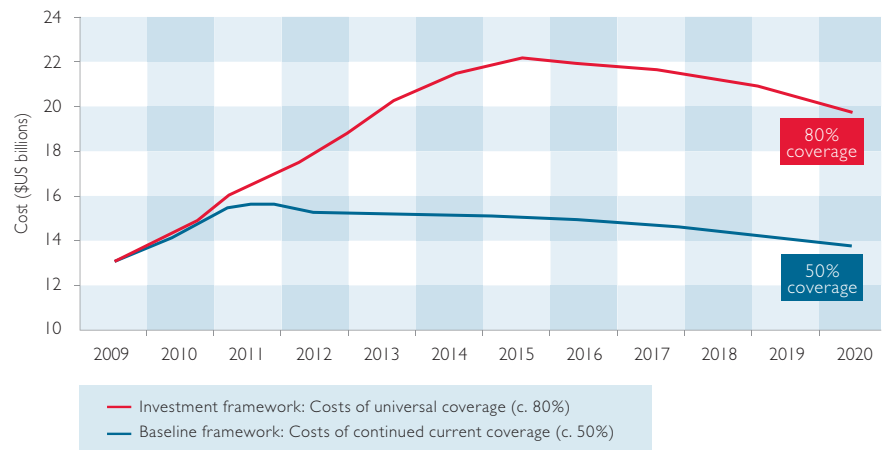
Combination antiretroviral treatment (ART) has radically changed the face of HIV infection, from a lethal disease into a chronic condition. Nevertheless, antiretroviral regimens are indeed costly and difficult for patients. Side-effects associated with years of ART uptake can be severe, while meticulous life-long adherence to ART is essential for the success of treatment, in particular to prevent viral resistance.

Moreover, there is an emerging consensus that persistent HIV infection is harmful even for treated patients who sustain undetectable viral load. The subsequent inflammation and chronic immune activation contributes to increased risk of cardiovascular disease, cancer and accelerated aging in patients living with HIV. Even in successfully treated patients, normal life expectancy is not fully restored. Moreover, a cure would allow people living with HIV to be freed of the stigma and discrimination, as well as fear of transmission, that are associated with HIV, which is one major impediment to the well-being of people living with HIV.

In addition to the individual benefit, recent scientific evidence has brought concrete proof that optimal ART can prevent HIV transmission at the population level through viral suppression in HIV infected patients. Therefore, finding novel therapeutic options in which patients would discontinue ART, and HIV would remain permanently undetectable should also have additional public health benefits by reducing HIV incidence.

## Substantial ART Cumulative Costs

Annual AIDS investment requirements for universal coverage of prevention, treatment, care and support



Within the next decade, most of the 34 million people currently living with HIV will, according to the current eligibility criteria of <500 CD4 cell count, require treatment; the total number of people eligible for treatment continues to expand.

UNAIDS estimates that there was a US \$10 billion shortfall in 2010 for a comprehensive and effective AIDS response. At the end of 2010 an estimated 7.6 million treatment-eligible people were not receiving life-saving ART, and this number will grow unless concerted action is taken. It is estimated that for every three people who started treatment in 2010, 5 more became newly infected.

Although the cost of delivering antiretroviral drugs has decreased substantially, and their availability in resource-poor settings has steadily increased, this continued effort to

expand access to the growing number of infected individuals is straining the resources of those organizations and countries where the epidemic is striking the hardest. Furthermore, as resistance develops over time – in relation with reduced adherence – a growing number of patients will need to switch from standard regimens to more expensive new generation medicines, resulting in a drastic increase of treatment costs.

Given the current economic situation, the life-long sustainability of treatment roll-out is threatened. The need for investment in short-course and more effective treatment strategies is critical to achieve at least long-term remission for patients. It is a humanitarian imperative both in terms of the individual and public health benefits, as well as an opportunity to potentially avoid the long term cumulative costs of ART.

“ Novel short-course treatment strategies allowing life-long drug-free remission of patients will bring individual, global and economical benefits. ”

Increased investments will not only aid in the search of an HIV cure, but can also contribute to advances in the HIV vaccine field and benefit public health globally, such as finding innovative treatments for people with cancer, Alzheimer's disease, other infectious diseases and immune disorders. HIV research also benefits the diagnostic field, it brings new approaches to the design of clinical trials, and innovative behavioural and social interventions.

# Why do we think a cure is feasible?

Today, our understanding of the mechanisms of HIV persistence and latent viral reservoirs is much better than it was a decade ago. The scientific community now agrees that it should be possible to at least find a functional cure for HIV/AIDS.

Recently, the first ever patient apparently cured from HIV infection was medically documented following complex medical interventions including a stem cell bone marrow transplant. Since then he has remained off ART with no viral rebound. A cure is therefore possible, although this type of intervention would not be applicable on a large scale. We have also gained a better understanding of the so-called “elite controllers”; individuals who have been infected with HIV for an extended period, but whose immune systems have controlled the infection without therapy and without symptoms.

To ensure effective outcomes to this research, the IAS is guiding the development of a Global Scientific Strategy, “Towards an HIV Cure”, which will be released in conjunction with AIDS 2012;

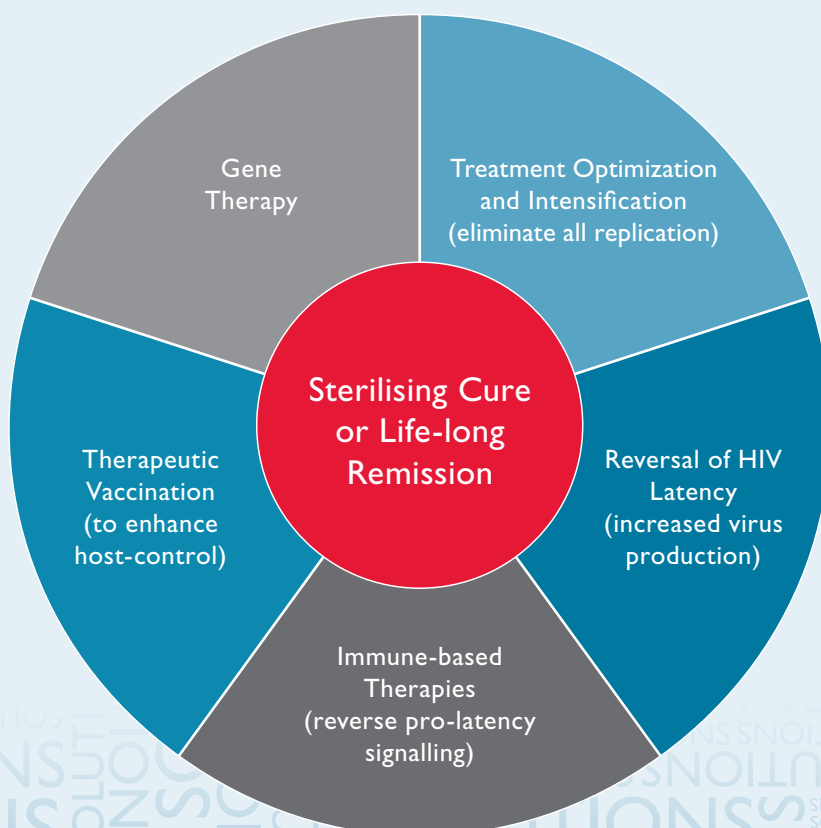
the XIX International AIDS Conference in Washington, D.C. in July 2012. It aims at contributing to the establishment of an international research alliance and global coordination of existing consortia towards an HIV cure. This strategy, taking a bottom-to-top approach, is prepared by an International Scientific Working Group composed of key experts in this area, in cooperation with an Advisory Board composed of research funders, patients’ representatives, clinicians from most affected countries and international organizations. It provides a strategic analysis of the state of research in the area of HIV persistence and eradication in order to develop recommendations for future studies and to promote international and cross-disciplinary research cooperation.

## How can we cure HIV?

It is expected that all these strategies will be more efficient in combination with each other, alongside the use of antiretroviral therapy to at least protect the immune system of patients to prepare them for a cure.

For more information on the project, its working group and advisory board, connect to [www.iasociety.org](http://www.iasociety.org)

Currently, the following strategies are being investigated:





# The road towards a cure

## The successful implementation of this plan will also require:

- Improved scientific collaborative research teams and institutions at the international level to ensure an optimal use of resources
- Cross-fertilisations of disciplines, in particular between clinical and basic science, both from the bench to bedside and from bedside to bench
- Platforms to facilitate data exchange between small pilot clinical trials, and standardisation of experimentation in primate models
- Training and research financing programmes created to enable young researchers and researchers from outside of the HIV field to bring innovative, out-of-the-box thinking to the area of HIV cure research
- Cooperation between the public research sector and the private sector, including regulatory agencies, to foster scientific discovery and translate it effectively into benefits for patients, accelerating the drug development pipeline for promising strategies
- Strong community engagement. It is important both to inform and prepare patients for participation in potential cure clinical trials with their fully informed consent, as well as to inform clinical trials designers on the needs of patients.

To do so, we recommend fostering the creation of a multidisciplinary international research alliance, with representation from all stakeholders involved in HIV cure research.

## To make substantial progress towards a cure for HIV, investments should be made in the following priority research areas:

- A. Determine the cellular and viral mechanisms that maintain HIV persistence. This includes defining the role of mechanisms that contribute to the establishment and maintenance of latent infection, as well as defining the role of viral replication and or homeostatic proliferation
- B. Determine the tissue and cellular sources of persistent HIV in long-term ART-treated individuals
- C. Determine the origins of immune activation and inflammation in the presence of ART and their consequences for HIV persistence
- D. Determine host and immune mechanisms that control infection but allow viral persistence
- E. Study, compare, and validate assays to measure persistent infection
- F. Develop and test therapeutic agents or immunological strategies to safely eliminate latent infection in individuals on ART. This includes strategies aimed at clearing latency
- G. Develop and test strategies to enhance the capacity of the host response to control active viral replication.

## References:

- Definition (Source: NIH, Office of AIDS Research) Research conducted on viral latency, elimination of viral reservoirs, immune system and other biological approaches, as well as therapeutic strategies that may lead to either a functional (control of virus rather than elimination, without requirement for therapy) or sterilising (permanent remission in absence of requirement for therapy) cure of HIV infection.
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Under no circumstances should the inclusion of "cure" in the global response direct funding away from treatment, prevention and care programmes, or from biomedical research on HIV and its consequences, including vaccine and other prevention research. However, it is imperative that donors, governments and the AIDS community make a viable economic investment in HIV cure research, and right now.