Global Investment in HIV CURE Research and Development 2014

Building the global investment and infrastructure to accelerate research towards a cure for HIV
Antiretroviral treatment (ART) has radically changed the face of HIV infection, from a lethal disease into a manageable chronic condition.

Most of 35 million people currently living with HIV will require ART within the next decade, and there are currently 26 million people in need of ART based on WHO 2013 Guidelines. At the same time, daily antiretroviral regimens are costly and difficult for patients and most importantly not curative. HIV persists despite even the best treatment, and contributes to the development of non-AIDS morbidity.

As such, it is time to strengthen our investments in the search for an HIV cure. Over the last decade, our understanding and knowledge of the mechanisms of HIV persistence and latent viral reservoirs has greatly improved. Many members of the scientific community now agree that the search for a functional cure or remission for HIV/AIDS may be within reach. Indeed, the past year has seen important new developments in the area of cure research:

- Ongoing and new studies to examine if earlier HIV suppression by ART is associated with significantly smaller HIV reservoirs and virologic control in adults and infants.
- Results from new trials of HIV latency-reversing agents and new studies to examine the potency of combinations of HIV latency-reversing agents.
- Results from the first trials using broadly neutralizing antibodies for therapeutic use and viral suppression in humans.

Despite these and other encouraging results, the scientific challenges remain important, as exemplified by the challenges faced by researchers’ unsuccessful attempts to replicate the results achieved for Timothy Brown, the only documented person to be cured of HIV, using bone marrow or peripheral blood stem cell transplants in other patients.

To ensure effective future outcomes for cure research, the International AIDS Society (IAS) developed a Global Scientific Strategy, which was launched in July 2012. The Global Scientific Strategy supports the establishment of an international research alliance and global coordination of existing consortia towards an HIV cure. It also 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.

To make substantial progress towards a cure for HIV, the IAS Global Scientific Strategy: Towards an HIV Cure, identifies the following priority research areas:

- Cellular and viral mechanisms that maintain HIV persistence
- Tissue and cellular sources of persistent SIV/HIV in animal models and long term ART-treated individuals
- Immune activation and dysfunction in the presence of ART
- Natural models of HIV/SIV control
- Assays to measure persistent infection
- Therapeutic and immunological approaches for eliminating persistent HIV infection
- Enhancement of immune response to control viral replication

Increased investments in these areas will aid in the search of an HIV cure, but can also contribute to increased knowledge of HIV pathogenesis and control, 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.

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**TOWARDS AN HIV CURE PROGRAMME DEFINITION: US NIH ERADICATION OF VIRAL RESERVOIRS***

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 sterilizing (permanent remission in absence of requirement for therapy) cure of HIV infection.

**Pathogenesis Studies**
Basic research on viral reservoirs, viral latency, and viral persistence, including studies on genetic factors associated with reactivation of the virus, and other barriers to HIV eradication.

**Animal Models**
Identification and testing of various animal and cellular models to mimic the establishment and maintenance of viral reservoirs. These studies are critical for testing novel or unique strategies for HIV reactivation and eradication.

**Drug Development and Preclinical Testing**
Programs to develop and preclinically test new and better antiretroviral compounds capable of entering viral reservoirs, including the central nervous system.

**Clinical Trials**
Studies to evaluate lead compounds, drug regimens, and immune-based strategies capable of a sustained response to HIV, including clinical studies of drugs and novel approaches capable of eradicating HIV-infected cells and tissues.

**Therapeutic Vaccines**
Design and testing of vaccines that would be capable of suppressing viral replication and preventing disease progression.

**Adherence/Compliance**
Development and testing of strategies to maintain adherence/compliance to treatment, in order to improve treatment outcomes and reduce the risk of developing HIV drug resistance.

In 2013, the IAS HIV Cure resource tracking group joined forces with the HIV Vaccines and Microbicides Resource Tracking Working Group (Working Group) to estimate global investments in HIV cure research. To date, this collaboration has yielded estimates for investment in 2012, 2013 and 2014.

The Working Group estimates that in 2014, US$157.9 million was invested in cure research, representing a substantial increase of 53% over the US$102.7 million invested in 2013, and an increase of 79% over the US$88.1 million invested in 2012. The majority of investments (US$139.9 million) came from the public sector with US$17.0 million invested by philanthropies such as Aides Fonds, amfAR, the Campbell Foundation, the Bill and Melinda Gates Foundation, Sidaction and the Wellcome Trust. Despite outreach by the Working Group this year, industry did not reply to the survey, as such this estimate undercounts commercial investment in cure research. Several companies are known to have active cure research programs including Gilead, BMS, Janssen, Merck and Sangamo BioSciences, among others.
Investment in Cure Research: 2014 shows a positive trend for HIV cure funding
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In 2014, the United States through the US National Institutes of Health contributed the majority of public funding, with the European Union, France, the United Kingdom, Australia, Switzerland and Canada also being significant contributors to HIV cure research.

The successful implementation of the Global Scientific Strategy plan will require improved international scientific collaborative research teams and institutions at the international level to ensure an optimal use of resources. Recent initiatives include:

- **IAS Towards an HIV cure initiative**
  In 2014, over 40 candidates were supported to attend the IAS symposium through the scholarship program. At the end of 2014, a new international scientific working group was convened to update and revise the IAS Towards an HIV cure Global Scientific Strategy. The revised Global Scientific Strategy will be launched in Durban at the occasion of the AIDS 2016 conference.

- **UNC Chapel Hill-GSK**
  A unique public-private partnership is creating a dedicated HIV cure center and a new company, Qura Therapeutics. GSK will invest $4 million per year for five years to accelerate the search for HIV cure and will also contribute personnel to UNC Chapel Hill.

- **amfAR Countdown to a Cure for AIDS**
  amfAR plans to strategically invest $100 million in cure research over the next 6 years aimed at finding a broadly applicable cure for HIV by 2020.

- **The HIV Cure Initiative.**
  Resulting from the Annenberg Foundation Trust “Summit on Public-Private Partnerships for Research Toward a Cure” in November 2013, the Initiative is an international alliance of scientific, governmental, philanthropic, and industry organizations launched in 2014 to identify, test, and distribute interventions that will lead to a cure. IDRI is currently serving as the fiscal sponsor of the Initiative.

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.

**Methodology**

Data collection was undertaken by AVAC on behalf of the HIV Vaccines and Microbicides Resource Tracking Working Group accessing public information and collecting information through direct appeals to funding agencies. Requests were made to the public, industry and philanthropic sector funders requesting information on cure research grants awarded in 2014 using the definition developed by the US National Institutes of Health’s Office of AIDS Research. The OAR definition is somewhat different than the research priorities in the Global Scientific Strategy excluding research into natural models of HIV/SIV control and including certain studies related to adherence to treatment. In early 2015, surveys were sent to several dozen potential cure research funders across the globe. Responses from funders may not be comparable due to subjective determinations of whether specific grants fall within the OAR definition of cure research. Some funders also decline to provide information, and some did not always provide grant specific detail. In reviewing responses, the Working Group accepted funders’ designation that specific research programs or grants came with the OAR definition.
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The HIV Vaccines and Microbicides Resource Tracking Working Group, for which AVAC acts as Secretariat, also includes the International AIDS Vaccine Initiative and the Joint United Nations Programme on HIV/AIDS.