Global Investment in HIV Cure Research and Development in 2013

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

Most of the 35 million people currently living with HIV will require ART within the next decade, and there are currently 16.2 million people in need of ART based on WHO 2013 Guidelines. Nevertheless, 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 have greatly improved. Many members of the scientific community now agree that the search for a functional cure for HIV/AIDS may be within reach. Indeed, the past year has seen important new developments in the area of cure research:

- Research suggests earlier HIV suppression by ART is associated with significantly smaller HIV reservoirs in perinatally infected infants. At least one infant infected with HIV who was treated immediately after birth has no signs of the virus.
- Ongoing studies in adults demonstrate that early initiation of ART is associated with a significantly lower HIV reservoir and in some cases the absence of HIV rebound after stopping ART.
- Results from the first trials of an HIV latency-reversing candidate, the HDAC inhibitor, showed safety and some effectiveness in activating virus.

Despite these and other encouraging results, the scientific challenges remain important, as exemplified by the two Boston patients heterozygous for CCR5-Δ32 with HIV who received stem cell transplants to treat cancers who saw viral rebound some time after treatment interruption.

To make substantial progress towards a cure for HIV, the IAS Global Scientific Strategy identified 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.

TOWARD A CURE PROGRAM 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.

Investment in Cure Research in 2013

In 2013, the United States (US), through the US National Institutes of Health contributed the majority of public funding, with France, the European Union, Australia and Canada also being significant contributors to HIV cure research. US investment is expected to increase in future years after President Obama announced in 2013 that $100 million of funding for the NIH would be reprioritized to enhance HIV cure research.

In 2012, non-US countries invested 11% of global HIV cure research funding, while in 2013, it is noted that the rest of the world increased proportionally their investment up to 16% of global HIV cure research funding, suggesting encouragingly that HIV cure research investment is expanding and non-US countries are increasing their funding.

The successful implementation of the Global Scientific Strategy plan will require improved scientific collaborative research teams and institutions at the international level to ensure an optimal use of resources. Encouragingly, there is investment in several international collaborations such as the Collaborative HIV Eradication of Viral Reservoirs (CHERUB) in the UK, the amfAR Research Consortium on HIV Eradication (ARCHE), the IAS/ANRS Young Investigator Award Program and the Martin Delaney Collaboratories.

**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 2013 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 2014, 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.
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 and 2013.

The Working Group estimates that in 2013, US$102.7 million was invested in cure research, an increase of 16% over the US$88.1 million invested in 2012. The majority of investments (US$98.5 million) came from the public sector with US$4.2 million invested by philanthropies such as Aides Fonds, amfAR, the Campbell Foundation and Sidaction. 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, Janssen, Merck and Sangamo BioSciences, among several others.

### INVESTMENTS IN HIV CURE RESEARCH BY FUNDER

#### 2012 Funding

**US$88.1 million**

- **amfAR**: 2.5
- **ANRS**: 3.5
- **Australian Research Council (ARC)**: 0.7
- **Australian National Health and Medical Research Council (NHMRC)**: 1.9
- **Bill & Melinda Gates Foundation**: 0.4
- **California Institute for Regenerative Medicine**: 7.6
- **Canadian HIV Vaccine Initiative (CHVI)**: 0.02
- **Canadian Institutes of Health Research (CIHR)**: 0.1
- **Center for Genetic Engineering and Biotechnology of Cuba (IGBC)**: 0.08
- **European Commission (EC)**: 1.6
- **Research Foundation Flanders (FWO)**: 0.05
- **Sangamo BioSciences, Inc.**: 8.9
- **Swedish Research Council (SRC)**: 0.2
- **Swiss National Science Foundation (SNSF)**: 0.3
- **UK Medical Research Council (MRC)**: 0.03
- **US National Institutes of Health (NIH)**: 60.0

#### 2013 Funding

**US$102.7 million**

- **Aids Fonds**: 0.7
- **amfAR**: 2.8
- **ANRS**: 6.8
- **Australian Research Council (ARC)**: 0.6
- **Australian National Health and Medical Research Council (NHMRC)**: 1.0
- **California Institute for Regenerative Medicine**: 7.5
- **Campbell Foundation**: 0.2
- **Canadian Foundation for AIDS Research (CANFAR)**: 0.02
- **Canadian Institutes of Health Research (CIHR)**: 0.7
- **European Commission (EC)**: 4.2
- **Fundação Calouste Gulbenkian**: 0.001
- **Ontario HIV Treatment Network**: 0.3
- **Research Foundation Flanders (FWO)**: 0.08
- **SIDACTION**: 0.1
- **Swiss National Science Foundation (SNSF)**: 2.0
- **US National Institutes of Health (NIH)**: 75.4
- **Wellcome Trust**: 0.3

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**Investment in Cure Research in 2013**

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Investment in Cure Research in 2013

INVESTMENTS IN HIV CURE RESEARCH BY COUNTRY

2012 Funding
US$88.1 million

2013 Funding
US$102.7 million

Australia 0.05 0.08
Belgium 0.4 0.9
Canada 0.08
Cuba 0.08
EC 1.6 4.2
France 3.5 6.8
Portugal 0.001
Sweden 0.2
Switzerland 0.03
UK 0.03 0.03
US 79.4 85.9

US
France
EC
Belgium
Australia
Switzerland
UK
Canada
Philanthropic
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