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AVAC

An Exploratory Analysis of HIV Treatment Research and Development Investments in 2009

July 2011

The HIV Treatment Research and Development Resource Tracking Project is a collaborative initiative of Treatment Action Group (TAG) and AVAC, directed and managed by TAG, in collaboration with UNAIDS.

About TAG
Treatment Action Group (TAG) is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS.

TAG works to ensure that all people with HIV receive lifesaving treatment, care, and information. We are science-based activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action on the part of all affected communities, scientists, and policy makers to end AIDS.

About AVAC
AVAC is an international nonprofit organization that uses education, policy analysis, advocacy, and community mobilization to accelerate the ethical development and eventual global delivery of new HIV prevention options as part of a comprehensive response to the pandemic. AVAC is also the secretariat of the HIV Vaccines and Microbicides Resource Tracking Working Group.

About UNAIDS
UNAIDS, the Joint United Nations Programme on HIV/AIDS, is an innovative partnership that leads and inspires the world in achieving universal access to HIV prevention, treatment, care and support.

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Foreword: Why HIV Treatment Research Is Critical to Ending the Pandemic

By Mark Harrington

> *I see unmet needs in two ways—unmet scientific needs and unmet implementation needs. One is as important as the other. The implementation need now has an impact on the scientific need. . . . We are starting to get very good cumulative data on discordant couples—where the infected partner is treated and not only is it good for them, but it prevents them from infecting the HIV-negative sexual partner. We have cohorts in cities, like Vancouver and San Francisco, where they are universally treating everybody and you see a correlation between treatment and the levels of infection in the community. . . . It depends when you want to spend the money. You can spend it now and put your arms around the epidemic and change the kinetics of it so you don't have 1.8 million people dying every year and 2.8 million people infected every year. You need to seek, test and treat, and link all of them to care. If you don't put in the money now, sooner or later you are going to have to pay at the end of the spectrum. And if you do that, at the end of the day, the amount of money spent is going to be much more. I am totally sensitive to the financial constraints we have, but I believe in the big picture of things, investing more money now is the way to go.*
>
> —Dr. Anthony S. Fauci, Director U.S. National Institute of Allergy & Infectious Diseases, National Institutes of Health, "Anthony Fauci reflects on 30 years of AIDS," *Science Speaks: HIV & TB News*, 17 May 2011

Last year UNAIDS called for a revolution in HIV prevention along with a radically simplified and easier to scale-up strategy called Treatment 2.0 (UNAIDS 2010a, 2010b). It is increasingly clear that the pathway to these two goals depends on accelerating and intensifying AIDS prevention and treatment research, which are increasingly integrated and vitally dependent on the same tools, including safer and more effective antiretroviral therapy (ART).

Research is bringing us tools that, for the first time, when used appropriately, have the promise to dramatically reduce new HIV infections while saving the lives of virtually all those infected with HIV who have access to high-quality and lifelong ART.

With the exception of condoms, needle exchange/harm reduction, and male circumcision, all these new HIV prevention tools are based on drugs initially developed for HIV treatment. With last year's groundbreaking studies of 1% tenofovir gel, applied vaginally twice a day by sexually active heterosexual women in South Africa (Abdool Karim et al. 2010), and of once daily oral Truvada (tenofovir/3TC), taken by men who have sex with men and transgender

persons in six countries, scientists proved for the first time that topical and oral ART can prevent sexual transmission of HIV (Grant et al. 2010).

Most recently, on 17 May 2011, the HIV Prevention Trials Network (HPTN), funded by the U.S. National Institutes of Health (NIH), announced the early results of HPTN 052, a randomized study of immediate (between 350 and 550 CD4 cells/mm^3) versus deferred (to CD4 cells/mm^3 <250) ART taken by the HIV-positive partner in 1,763 serodiscordant couples. The Data and Safety Monitoring Board recommended that study results be disseminated at once and deferred-arm partners offered immediate ART after it found the partners of the recipients who received ART early experienced a staggering 96% reduction in HIV acquisition (one case in the early ART arm versus 27 cases in the deferred arm, when infection was matched by source virus). An additional benefit to the HIV-positive early enrollees was a reduction in all morbidity and mortality events (40 in the early therapy arm vs. 65 in the deferred) and in deaths (10 in early vs. 13 in deferred), and a statistically significant 85% reduction (3 cases in early vs. 17 in deferred) of extrapulmonary tuberculosis, a difficult-to-treat and often fatal complication of HIV infection (National Institutes of Health 2011a, 2011b).

Further trials now underway will more accurately quantify the benefits of earlier initiation of ART and the impact of "test-and-treat" or "test, link, and care" strategies on morbidity, mortality, and HIV transmission.

What is obvious from these studies, however, is that both the preventive and the therapeutic benefits of HIV treatment depend vitally on adherence, which in turn depends on the adequacy of the health system, sufficient funding, HIV treatment and prevention literacy among those receiving the services, and the tolerability, ease of use, lack of toxicity, and sufficient barrier to the emergence of resistance of the treatment modalities used. When adherence was high, as in HPTN 052, the benefits to both HIV-negative and HIV-positive partners were unparalleled. When adherence was mixed, as in iPrEx and CAPRISA 004, only those able and willing to tolerate long-term use of the dual oral pill or the vaginal gel, respectively were able to benefit from the intervention.

We have a long way to go if we are to meet the new global treatment target of 15 million by 2015 and carry out the prevention revolution that these new research results demand—and that UNAIDS and the World Health Organization (WHO) called on countries to implement in 2010.

Executive Summary

This report is a preliminary assessment of global investments in research and development (R&D) devoted to the discovery and development of new therapies and treatment strategies for HIV. As part of a broader effort to track and analyze HIV/AIDS spending, UNAIDS commissioned the Treatment Action Group (TAG) and AVAC to measure global R&D spending for HIV treatment, starting with the year 2009.

From a total of 144 surveyed institutions, 48 funders reported investing $2.5 billion in HIV treatment R&D in 2009. The scope of HIV treatment R&D included HIV basic science, drug discovery, drug development, diagnostics, and operational and implementation science on antiretroviral therapy, primary HIV-associated coinfections, opportunistic infections and cancers, other HIV-associated diseases, immune-based therapies, and therapeutic vaccines.

Using 2009 as the baseline year, TAG collected data using electronic surveys from public, private, philanthropic, and multilateral funding institutions. Funders were asked to report their HIV treatment research awards and classify them according to six predefined research areas: basic science; applied/infrastructure/unspecified; diagnostics; drug discovery and development; antiretroviral therapy (ART) prevention; and operational and implementation science.

The following summarizes the report's key findings:

- Forty-eight funders worldwide reported investing $2,461,546,974 or approximately $2.5 billion in HIV treatment–related research in 2009.

- Public-sector funders accounted for the largest share of HIV treatment R&D spending in 2009 at $1.8 billion (73%), followed by $591 million (24%) from the private sector—an incomplete figure due to the low industry response rate, $39 million (2%) from multilateral agencies, and $31 million (1%) from the philanthropic sector.

- Across the six HIV treatment research areas, research to discover and develop new drugs or optimize existing drugs to treat HIV infection and its related comorbidities received 51% of overall HIV treatment R&D funding. Basic science received the second largest share (32%), followed by operational and implementation science (13%), ART prevention (3%), applied/infrastructure/unspecified (1%), and diagnostics (0.1%).

TABLE 1

HIV Treatment R&D Funding by Research Area

Research Area	2009 Funding	Percent
Drug Discovery & Development	$1,249,043,852	50.7%
Basic Science	$787,155,521	32%
Operational & Implementation Science	$307,702,581	12.5%
ART Prevention	$84,887,996	3.4%
Applied/Infrastructure/Unspecified	$30,649,011	1.2%
Diagnostics	$2,108,014	0.1%
Total	**$2,461,546,974**	

- The NIH was the largest funder across four research areas—basic science, drug discovery and development, operational and implementation science, and ART prevention—and the leading investor worldwide in HIV treatment R&D, investing $1.6 billion in 2009 (two-thirds of the reported total).

- Despite active therapeutic clinical activity sponsored or cosponsored by the private sector in 2009 (see Tables 5 and 6 on pages 29 and 30), only 11 out of 46 private-sector companies responded to the survey request. Seven companies provided funding data, three confirmed that HIV treatment R&D was not a funding priority, and one declined to participate. Since only a small segment of industry investments for HIV treatment R&D were captured in this report, the private-sector figure is clearly incomplete.

- The 48 participating HIV funders in this report are based in 18 donor countries, with institutions based in the United States providing 92%, or $2.26 billion, of the total investment.

This report marks the beginning of an ongoing effort to annually monitor worldwide investments in HIV treatment research. It is meant to complement work done by the HIV Vaccines and Microbicides Resource Tracking Working Group, which has tracked HIV prevention research funding since 2004.

Increased funding for HIV drug discovery and development has never been more urgent. Recent and emerging recommendations to start ART earlier, for both prevention and treatment, means that new drug regimens must be simpler, less toxic, resilient, more forgiving of treatment interruptions, less prone to promote the emergence of drug resistance, require lower dosages, and have fewer interactions with other drugs commonly used by people with HIV. To secure new and sustain existing investments for improved HIV drug treatment, it is necessary to know who is investing what, where, and why. This report establishes a baseline of reported HIV treatment R&D funding from 2009 and will supplement existing resource-tracking efforts to provide a more comprehensive overview of worldwide investments in HIV research and development.

1. Introduction

Throughout the first three decades of the HIV pandemic there was no comprehensive data measuring the world's aggregate investment in R&D devoted to discovery and development of new therapies and treatment strategies for HIV. This report, developed by TAG and AVAC and supported by UNAIDS in 2010, is the first attempt to map the landscape of HIV treatment R&D investments, starting with the year 2009.

The discovery, development, and global scale-up of ART remains one of the greatest accomplishments of modern biomedical science and public health. Within the first 30 years of the global HIV pandemic, over 30 drugs and fixed-dose antiretroviral combinations have been approved for use by regulatory authorities in the United States, Europe, and other developed and developing countries. Of the world's 33.3 million people with HIV, approximately 6.6 million were receiving ART by the end of 2010 (UNAIDS 2011). Another 9 million need HIV treatment now (UNAIDS 2011), and the remaining 18 million who live with earlier stages of HIV infection will eventually need treatment. In addition, the 2.6 million individuals with new HIV infections each year will also ultimately need treatment. Ongoing studies will determine whether HIV therapy should start with diagnosis—regardless of CD4 cell count—and whether and by how much earlier initiation and broader uptake of HIV treatment reduces HIV transmission.

The World Health Organization (WHO) 2010 HIV treatment guidelines update, coupled with new and emerging data on the effectiveness of HIV therapy for prevention, add urgency to the search for new drugs and drug combinations. These new therapies will need to be as potent as existing ones, but less toxic, more forgiving of treatment interruptions, with a higher barrier to the emergence of resistance, and with fewer interactions with other drugs commonly used by people with HIV, including treatments for tuberculosis (TB), the hepatitis B and hepatitis C viruses (HBV and HCV), and opioid substitution therapy, as well as forms of contraception. Ideally these new drugs or fixed-dose combinations (FDCs) would have long half-lives—enabling weekly or monthly dosing—and low molecular weight to reduce manufacturing costs.

Along with a vaccine, a cure is urgently needed to enable people with HIV to move beyond daily lifelong triple therapy to either a sterilizing cure (with HIV RNA, DNA, and proteins cleared from the body) or a functional cure (with no requirement for daily treatment). HIV treatment research now includes a growing emphasis on therapies that perturb the pool of latently infected CD4 T cells, but a successful search for a cure will need new emphasis, funding, and science.

Pending the discovery and development of a safe and effective HIV vaccine, it is clear that smart, evidence-based use of ART is among the most powerful tools for limiting the spread of the pandemic, preserving health, lengthening life, and preventing new infections. To make best use of existing HIV treatment while pursuing innovative drug design and simplification, UNAIDS and the WHO launched the Treatment 2.0 framework in 2010,

a long-term treatment strategy to achieve universal access to HIV prevention, treatment, care, and support. The framework entails five priorities: optimizing drug regimens, simplifying laboratory for diagnosis and treatment monitoring, reducing costs, adapting delivery systems, and mobilizing communities (Hirnschall & Schwartländer 2011). Implementation of this framework globally is likely to stimulate drug and diagnostic development, while implementing it at the country level will address some of the structural barriers that thwart the goal of universal access.

1.1 Rationale

In 2009, the number of people receiving ART grew by 30% from 4.1 million to 5.3 million. Yet, 2.6 million new infections and 1.8 million AIDS deaths occurred (UNAIDS/World Health Organization 2010). New infections continue to outpace the number of people placed on treatment by 2:1. This ratio is not fixed by fate but is due to continued uncontrolled spread of HIV combined with still inadequate scale-up. In 2009, for the first time in the decade, global investments in HIV prevention and treatment, "remained essentially flat over the 2008–2009 period . . . commitments from donor governments totaled US$8.7 billion, the same as in 2008 . . . [while] US$23.6 billion would have been necessary—from all sources, including domestic and international—for the global HIV response in low- and middle-income countries in 2009" (Kaiser Family Foundation/UNAIDS 2010). Inadequate and unreliable funding poses a significant threat to ensuring that those now receiving treatment are able to stay on it, while threatening to close off treatment to those who will need to start therapy over the coming years.

To measure progress and assess whether funding levels are adequate and properly invested in the most promising science, TAG and AVAC sought to document the world's investment in developing new or enhancing existing HIV therapeutic regimens and strategies by examining R&D spending and establishing an investment baseline based on 2009 data.

Monitoring investments in HIV is essential for understanding and measuring global progress to address HIV/AIDS and achieve universal access. The HIV Vaccines and Microbicides Resource Tracking Working Group (RTWG) has monitored HIV prevention R&D funding since 2004 and produces a comprehensive resource-tracking report used by researchers, policy makers, and advocates to provide an evidence base for policy advocacy on R&D investments for HIV vaccines, microbicides, and other prevention options (HIV Vaccines and Microbicides RTWG 2011). This report complements the work of the HIV Vaccines and Microbicides RTWG by collecting and reporting annual investments in HIV treatment research.

FIGURE 1

HIV Research and Development Overview

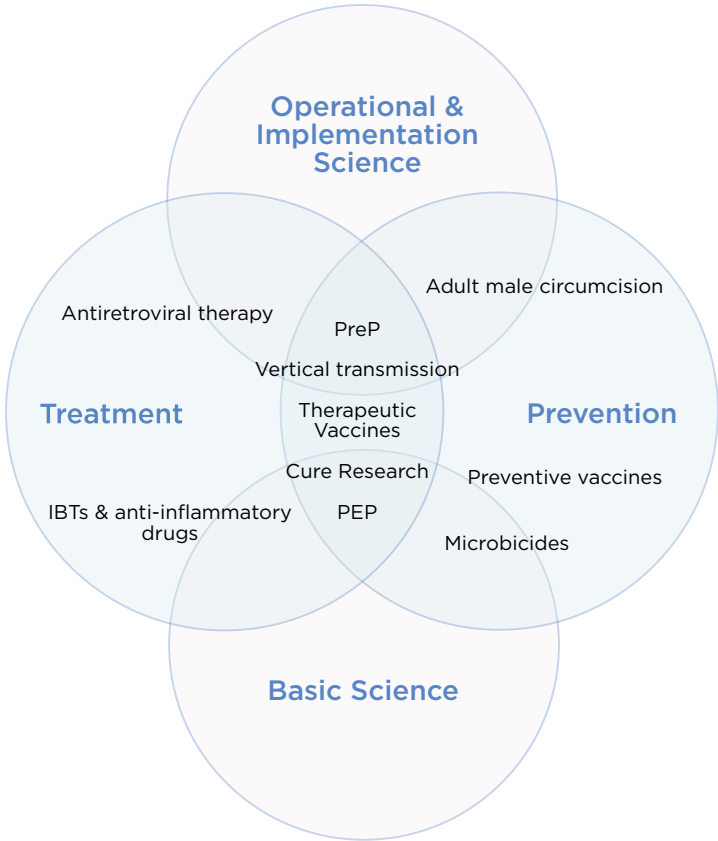


Figure 1 illustrates the different research areas that comprise a comprehensive HIV R&D agenda. The diagram shows how basic science serves as a foundation for both treatment and prevention research, how treatment-related research overlaps with HIV prevention science (e.g., preventing vertical transmission, ART prevention, therapeutic vaccines, preexposure prophylaxis, and postexposure prophylaxis), and the role of discovery, development, and operational and implementation science in validating the use of new interventions in programmatic settings.

With the roll out of the Treatment 2.0 framework, this report will contribute data relevant to two priority areas—radical simplification, and innovative drug design and diagnostics—by reporting on investments that keep the research pipeline active and monitoring country-level treatment related research spending.

1.2 Methodology

For this analysis, TAG solicited information from funders supporting research and development on basic, applied, and operational and implementation science related to treatment interventions and strategies for HIV (e.g., antiretroviral drugs); associated HIV coinfections (e.g., TB, HBV, and HCV); opportunistic infections (e.g., cytomegalovirus, *Pneumocystis*) and cancers (e.g., Kaposi's Sarcoma, non-Hodgkin's lymphoma); other HIV-associated diseases (among them chronic brain, bone, cardiovascular, kidney, and liver disease); immune-based therapies (IBTs); and therapeutic vaccines for HIV.

Based on desktop research and conversations with colleagues at AVAC, TAG identified 144 potential HIV treatment R&D funders. TAG solicited data using an e-mail survey and portfolio-reporting template to facilitate a uniform reporting process. Each funder was asked to report all of its HIV treatment research awards, primary recipients, amounts disbursed in 2009 (in specific currencies), and to specify whether the award was part of a multiyear project. Funders were asked to classify the awards according to six predefined research areas:

- **Basic science**: Research that uncovers or enhances fundamental knowledge about HIV virology, immunology, natural history, pathogenesis, and the immune response, but is not linked to a specific product or therapy.

- **Applied/infrastructure/unspecified**: Translational research specific to HIV treatment; funds to support research-related infrastructure; or research the funder is unable to categorize.

- **Diagnostics**: Research to discover and develop better, simpler, cheaper, and more accurate diagnostic tests to measure HIV RNA levels, CD4 counts, or drug-resistance mutations—any of which could simplify HIV care.

- **Drug discovery and development**: Research to develop new drugs or enhance existing compounds to treat HIV. Research includes drug discovery, preclinical, or clinical research on
    - —antiretroviral (ARV) drugs
    - —treatments for coinfections and opportunistic infections
    - —IBTs, including anti-inflammatory treatments and therapeutic vaccines
    - —other HIV-associated treatments

- **Antiretroviral therapy prevention**: Research aimed at understanding the use of ART, developed for therapeutic purposes, in circumstances where it may also have a prevention impact. For this report, ART prevention includes: PEP; the use of treatment to prevent HIV infection after exposure; prevention of vertical transmission through ART treatment; PrEP; the use of ART treatment regimens for key HIV-negative populations in order to prevent HIV acquisition; and a prevention strategy known as "test and treat" where ART treatment is scaled-up to

drive down new infections by reducing community-wide viral load. Specific funding levels for these interventions are not disaggregated in this report. A breakdown of global funding for PrEP and prevention of vertical transmission in 2009 can be found in the HIV Vaccines and Microbicides RTWG report *Advancing the Science in a Time of Fiscal Constraint: Funding for HIV Prevention Technologies in 2009*.[1]

- **Operational and implementation science**: research evaluating new and existing HIV therapeutic interventions and strategies to guide their effective implementation in program settings. Focuses include randomized trials, surveillance, and epidemiological and prospective observational studies.

Sixty-one of the 144 funders who received TAG's survey responded. Thirty-four provided 2009 HIV treatment R&D investment data, including seven private-sector companies. Sixteen institutions confirmed that HIV treatment R&D is not a priority funding area. Two did not fund HIV treatment research in 2009. Six funders—two public and four private—promised to complete surveys but did not do so by press time. Two public-sector funders were unable to participate because their reporting systems could not track or earmark funds, and one private-sector funder explicitly declined to participate in the survey. Eighty-three funders did not respond to the survey request.[2]

Of the 34 completed surveys, 29 came from original source funders and five from funding recipients. Recipient surveys uncovered 19 additional original source funders, for a total of 48 funders.

The 48 funders are based in 18 countries (see Figure 3). To compare and analyze data, TAG converted all non-U.S. currencies to U.S. dollars using the Oanda currency conversion site (http://www.oanda.com/currency/converter/) with the 1 July 2009 currency exchange rate.

1.3 Limitations

This report is the first resource tracking dedicated to global HIV treatment R&D. TAG and AVAC acknowledge that the data in this report capture only a portion of global investment in HIV treatment R&D. Several factors explain the limitations of the data and render our analysis subject to revision as more data emerge:

- Despite several attempts to collect data from the private sector, the response rate was low. Of the 46 private-sector companies asked to complete the survey, 7 provided funding data, 3 confirmed no longer investing in HIV treatment R&D, and 1 declined to participate; 35 companies remained unresponsive. Anticipating the private sector's concerns over sensitive proprietary or strategic investment information, TAG offered the option of publishing company investments by name or anonymously. Only 2 companies chose to provide data anonymous-

1. HIV Vaccines and Microbicides RTWG 2009. In 2011, the report will provide estimates for global investment in use of ART treatment in HIV-positive individuals to reduce community-wide viral load.
2. For a full listing of nonrespondents please see Appendix B.

ly (Company A and Company B). To illustrate the magnitude of the missing funding data, TAG summarized clinical trial activity in 2009 that was sponsored or cosponsored by the private sector (see Tables 5 and 6 on pages 29 and 30).

- While public-sector funders provided the bulk of data presented in this report, public-sector institutions in several major countries are missing from this report (e.g., China, Mexico, the Russian Federation, and South Africa). Two challenges in identifying a point of contact who has authority and access to an institution's disbursement data are: (1) establishing contact remotely and (2) relying on communication only in English or Spanish. In future reports, TAG and AVAC will continue to nurture existing relationships and foster new ones in order to build a solid network of contacts to participate in future surveys. If funding permits, TAG may translate the survey tool to increase the response rate.

- Of the 34 organizations that completed the survey, 85% were original source funders and 15% were funding recipients. Therefore, most data reflect disbursements rather than amounts received, which may differ due to changes in exchange rates, overhead charged by intermediary institutions, and other transaction charges. When TAG received data from a funder and a recipient, TAG deferred to recipient data whenever possible.

- Variations in fiscal calendars also create reporting challenges because some institutional funding cycles extend across calendar years. TAG deferred to the funder's fiscal year cycle.

- Originally, the survey used to collect funding data did not include the diagnostics research category. Even so, a few funders included diagnostic funding in their surveys. After careful consideration, TAG decided to include these data because diagnostics are closely linked to initiation and monitoring of ART. Because only a handful of funders voluntarily provided this data, diagnostics funding is underreported for 2009. TAG will improve the accuracy of these data in future reports by including diagnostics as a research category in the survey.

- Several public-sector funders, particularly development agencies, make large multiyear investments in health research, including operational and implementation science on HIV therapeutics. However, when asked to report on HIV-specific research investments, development agencies were unable to disaggregate their investments. Without standard earmarking or reporting practices these investments were difficult to incorporate into the global funding figure. TAG contacted grant recipients whenever possible to collect 2009 disbursement data and confirmed the amount with the original source funders.

- Resource tracking is an important tool in promoting transparency and accountability. In this era of fiscal austerity, it is imperative to know where funds are di-

rected and how they are used. Funders may be approached by several independent organizations to collect funding data, resulting in more than one request in a given year. To promote continued collaboration, TAG makes every effort to minimize requests and, if possible, collaborates with other organizations to collect the necessary information. Nevertheless, TAG believes that it is essential for policy makers and donors (governments, foundations, and companies alike), as well as researchers, advocates, providers, and public health practitioners, to know what is being funded, by whom, why, and for how long.

1.4 Corrections

TAG strives to report the most up-to-date information on HIV treatment R&D to inform the public and advance the field. If you would like to add or correct information or suggest changes to improve the accuracy of the data, please contact Eleonora Jiménez-Levi at eleonora.jimenez@treatmentactiongroup.org.

2. Results

TABLE 2

Top 48 Funders in HIV Treatment R&D in 2009, as Reported to TAG in 2010

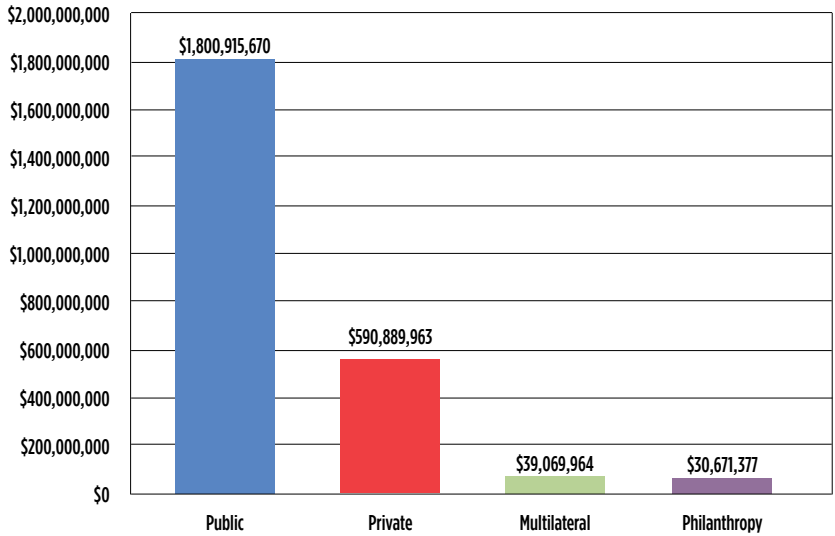
#	Funding Institution	Funder Type	Total (USD)
1	US National Institutes of Health (NIH)	P	$1,662,556,000
2	Gilead Sciences	C	$573,390,000
3	UK Medical Research Council (UK MRC)	P	$39,300,905
4	Agence Nationale de recherche sur le SIDA (ANRS)	P	$36,930,094
5	European Commission (EC)	M	$32,866,129
6	Canadian Institutes of Health Research-HIV/AIDS Research Initiative (CIHR)	P	$20,535,706
7	Wellcome Trust	F	$14,885,551
8	Bill & Melinda Gates Foundation (BMGF)	F	$11,583,996
9	UK Department for International Development (UK DFID)	P-D	$11,223,217
10	Australian National Health and Medical Research Council (Australia NHMRC)	P	$9,739,226
11	Company A	C	$8,000,000
12	Japan Ministry of Health, Labour and Welfare	P	$6,942,960
13	European & Developing Countries Clinical Trials Partnership (EDCTP)	M	$6,164,116
14	SEEK	C	$3,313,100
15	GeoVax Labs, Inc.	C	$3,045,823
16	amfAR	F	$2,315,330
17	Swedish Research Council (SRC)	P	$2,254,546
18	Italian Ministry of Health	P	$1,466,663
19	Brazil Ministry of Health, Dept. of STD, AIDS and Hepatitis	P	$1,422,363
20	Institute of Tropical Medicine (ITM)	P	$1,408,510
21	Australian Centre for Hepatitis and HIV Virology	P	$1,297,732
22	Esteve Pharmaceuticals	C	$1,290,000
23	Company B	C	$1,231,295
24	Indian Council of Medical Research (ICMR)	P	$811,462
25	Australian Research Council	P	$790,982
26	Swedish Foundation for Strategic Research (SFSR)	F	$779,760
27	Imperial College of Science, London	P	$735,358
28	Dutch Ministry of Foreign Affairs (DGIS)	P-D	$653,238
29	Cytheris	C	$619,744
30	Victorian Dept. of Human Services, Australia	P	$546,319
31	Flemish Government	P	$361,226
32	Bettencourt Schueller Foundation	F	$352,128
33	Italy Ministry of Foreign Affairs	P	$333,333
34	USAID	P-D	$304,449
35	Austria AIDS Life Association (AALA)/Life Ball	F	$277,859
36	Swiss Agency for Development and Cooperation (SDC)	P-D	$277,047
37	Research Foundation Flanders	P	$274,810
38	Doris Duke Charitable Foundation	F	$270,000
39	Institute for the Promotion of Innovation by Science and Technology	P	$265,072
40	New Zealand Health Research Council	P	$247,681
41	Canadian Foundation for AIDS Research (CANFAR)	F	$206,753
42	Federal Science Policy Office (BELSPO)	P	$102,910
43	World Health Organization (WHO)	M	$39,720
44	Family Health International (FHI)	P-D	$38,655
45	Indian National AIDS Control Organization	P	$36,510
46	Amsterdam School for Social Science Research	P	$28,189
47	Papua New Guinea Institute of Medical Research Fund	P	$22,056
48	Centrum voor Informatie en Samenlevingsopbouw VZW	P	$8,451
	Grand Total		**$2,461,546,974**

P = Public Sector Agency **P-D** = Public Sector Development Agency
F = Foundation/philanthropy **C** = Corporate/private sector
M = Multilateral Agency

2.1 Investments by Funding Sector

FIGURE 2

2009 HIV treatment R&D: Investment by Funding Sector



In 2009, funders reported investing $2.5 billion in HIV treatment research. Of those funds, $1.8 billion (73%) came from the public sector, $591 million (24%) from the private sector,[3] $39 million (2%) from multilateral agencies, and $31 million (1%) from philanthropic foundations.

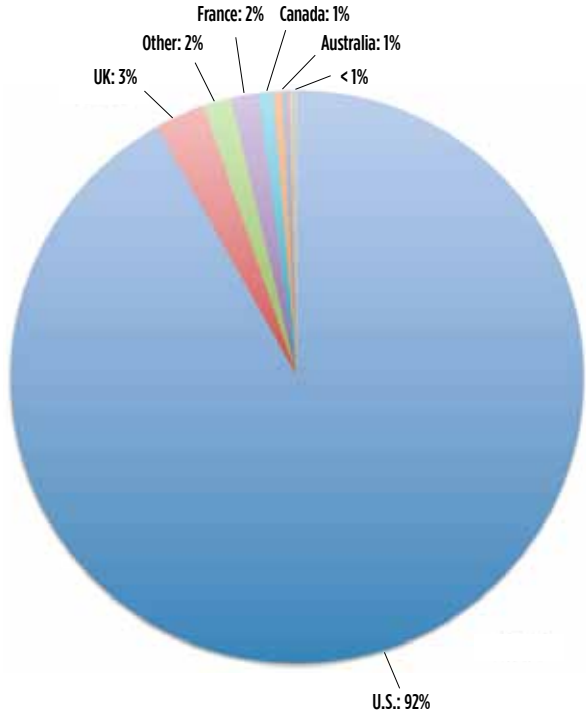
2.2 Geographic Location of Funding Institutions

The majority of HIV treatment R&D funding institutions reporting to TAG are based in high-income countries. Approximately $2.3 billion (92%) of HIV treatment funding came from the United States due to the large investments made by the NIH and Gilead Sciences. Data from middle- and low-income countries were limited, with only Brazil, India, and Papua New Guinea reporting investments. TAG believes that middle-income countries such as China, Mexico, the Russian Federation, and South Africa, among others, are investing in HIV treatment R&D but were simply not captured in this report.

3. Private-sector investment levels are significantly underreported since many pharmaceutical and biotechnology product sponsors did not respond to TAG's survey request.

FIGURE 3

2009 HIV Treatment R&D: Geographic Location of Public, Private, Multilateral, and Philanthropic Funding Institutions



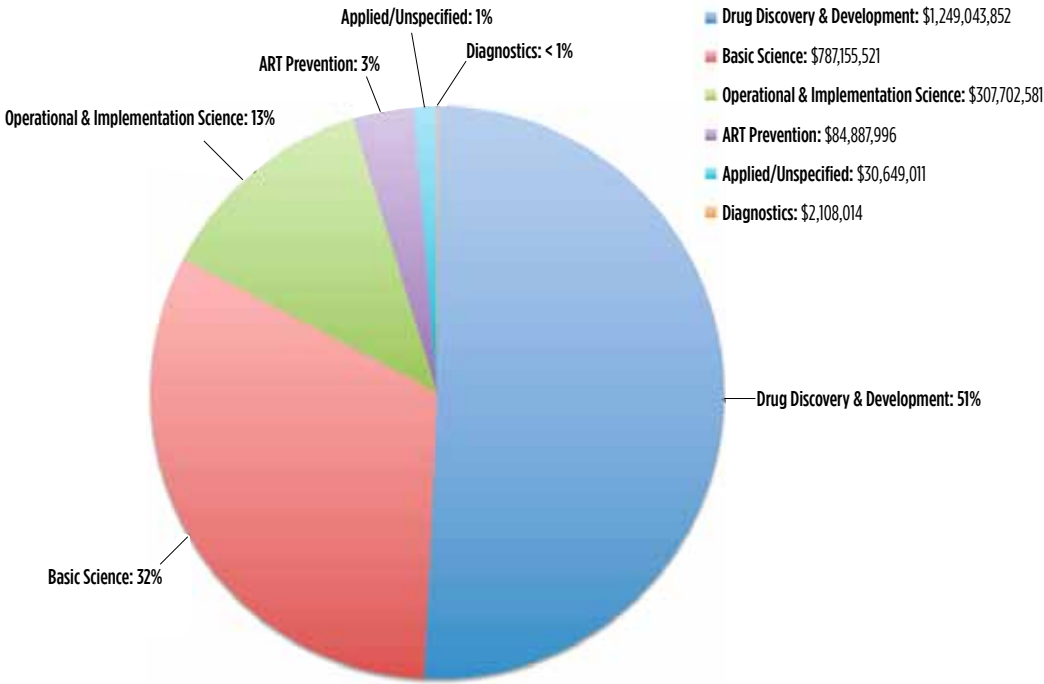
#	Funder Country of Origin	Total (USD)	#	Funder Country of Origin	Total (USD)
1	US	$2,261,504,254	10	Italy	$1,799,996
2	UK	$69,458,132	11	Brazil	$1,422,363
3	Other	$39,069,964	12	Spain	$1,290,000
4	France	$37,901,966	13	India	$847,972
5	Canada	$20,742,459	14	The Netherlands	$681,427
6	Australia	$12,374,258	15	Austria	$277,859
7	Japan	$6,942,960	16	Switzerland	$277,047
8	Belgium	$3,652,275	17	New Zealand	$247,681
9	Sweden	$3,034,306	18	Papua New Guinea	$22,056
				Grand Total	**$2,461,546,974**

2.3 Investments by Research Area

Drug discovery and development accounted for half (51%) of all HIV treatment R&D funding in 2009, followed by basic science (32%), operational and implementation science (13%), ART prevention (3%), applied/infrastructure/unspecified (1%), and diagnostics (< 1%).

FIGURE 4

2009 HIV Treatment R&D: Investment by Research Area



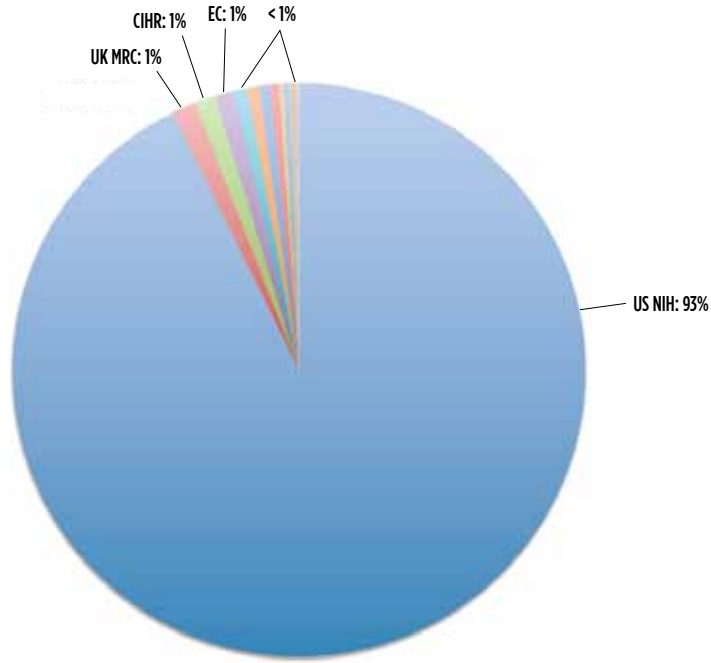
2.4 Basic Science

Reported investments in basic science essential for the discovery and development of new and better HIV treatment totaled $787 million in 2009, 93% of which was financed by the NIH. With an AIDS research budget of $3 billion in 2009, the NIH allocated the largest share to basic science (referred to by the NIH as etiology and pathogenesis research), reflecting the institution's commitment to expanding basic science research. Basic science sets the

foundation for product discovery and development and is predominantly financed by public-sector institutions. Without in-depth research on the biology and pathogenesis of HIV, advances in diagnostics, drug, and vaccine development would not be possible. Basic science research on HIV virology, immunology, and pathogenesis is also vital to discovering a cure for HIV infection.

FIGURE 5

Basic Science: 2009 Investments



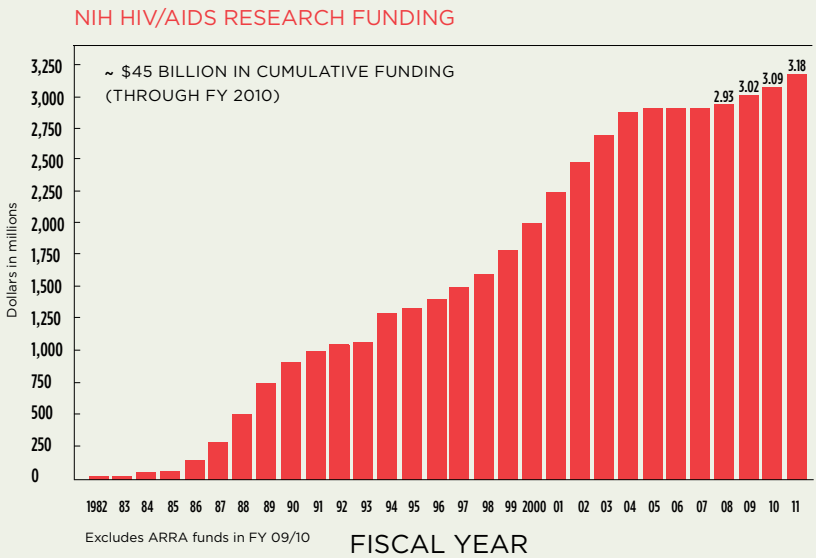
#	Funding Institution	Total (USD)	#	Funding Institution	Total (USD)
1	US NIH	$729,991,000	11	ITM	$1,408,510
2	UK MRC	$10,508,259	12	amfAR	$1,406,869
3	CIHR	$9,261,756	13	SFSR	$779,760
4	EC	$8,496,382	14	Australian Research Council	$417,052
5	NHMRC	$6,039,556	15	Doris Duke	$270,000
6	ANRS	$5,298,136	16	New Zealand HRC	$215,451
7	Wellcome Trust	$4,890,328	17	Brazil MoH	$144,104
8	BMBF	$3,999,736	18	CANFAR	$138,267
9	SRC	$1,907,033	19	ICMR	$134,089
10	Japan MoH	$1,849,232			
				Grand Total	**$787,155,521**

2.5 The NIH Office of AIDS Research Strategic Plan and Budget for AIDS Research

By far the largest investor in HIV research overall and in treatment R&D is the NIH. Since 1993, the NIH AIDS research effort has been under the oversight of the NIH Office of AIDS Research (OAR), which reports to the NIH director and plans, evaluates, budgets, and produces an annual NIH AIDS research strategy. Cumulatively, the NIH has invested almost $45 billion in HIV R&D since 1982.

TABLE 3

NIH Office of AIDS Research, Cumulative HIV/AIDS Research Funding 1982-2011



Source: Fauci 2011.
Note: ARRA = the American Recovery and Reinvestment Act.

The NIH AIDS research budget is distributed across a subset of 27 NIH institutes and centers according to scientific priorities, which are updated annually in the OAR strategic plan. The scientific research agenda is prioritized among and within the categories of etiology and pathogenesis; natural history and epidemiology; therapeutics; microbicides; vaccines; behavioral and social sciences research, training, infrastructure, and capacity building; and information dissemination.

TABLE 4

NIH Office of AIDS Research, Budget Authority by Program (in U.S. dollars)

Area of Emphasis	FY 2009 Actual
HIV Microbicides	$128,670,000
Vaccines	$560,956,000
Behavioral & Social Science	$434,305,000
Therapeutics	
Treatment as Prevention	*$84,775,000*
Drug Discovery, Development, & Treatment	*$585,786,000*
Total, Therapeutics	$670,561,000
Etiology & Pathogenesis	$729,991,000
Natural History & Epidemiology	$247,914,000
Training, Infrastructure, & Capacity Building	$198,028,000
Information Dissemination	$48,868,000
Total	**$3,019,293,000**

Source: Office of AIDS Research, National Institutes of Health 2011.
Note: Excludes funding from the American Recovery and Reinvestment Act (ARRA).

For this report, TAG included the full amounts invested in 2009 in etiology and pathogenesis ($729,991,000); natural history and epidemiology ($247,914,000); therapeutics research ($670,561,000), which includes drug discovery, development, and optimization; and therapeutic vaccine research ($14,090,000) which is budgeted under vaccines. The remaining $1.36 billion NIH AIDS research investment, outside the scope of this report, was directed to HIV microbicides; vaccines; behavioral and social sciences; training, infrastructure and capacity building; and information dissemination.

Though much if not all research on HIV etiology, pathogenesis, natural history, and epidemiology applies just as fully to prevention science as to treatment research, TAG felt it was essential to include these categories in the funding total since this exploratory and population-based science contributes important information to treatment discovery and development. Ultimately, TAG and AVAC would like to provide a complete picture of global HIV research by integrating data on prevention technologies, tracked by the HIV Vaccines and Microbicides RTWG, with therapeutic research data in this report.

2.6 Drug Discovery and Development

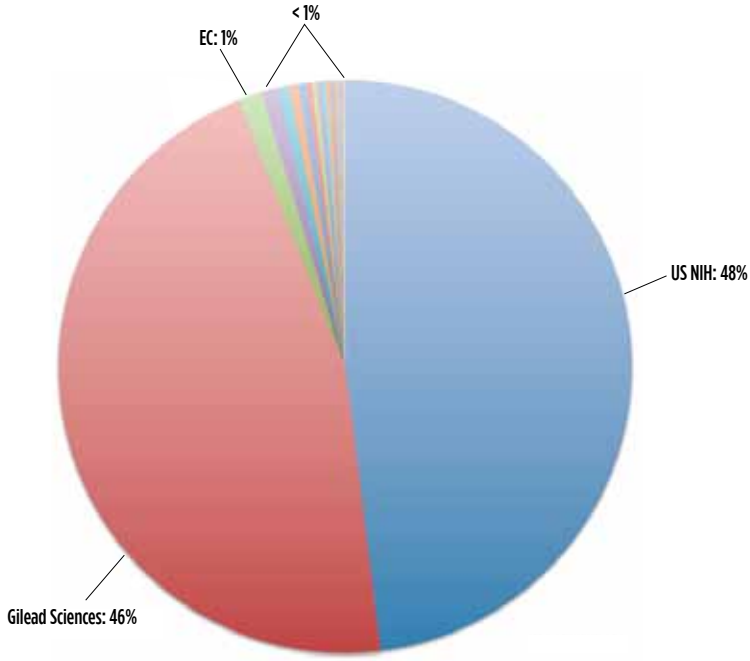
Total reported investment on HIV related drug discovery and development in 2009 was $1.2 billion. The NIH was the lead investor, spending $599 million toward discovering and developing new therapeutic approaches to HIV infection, including prevention and treatment of coinfections, cancers, treatment-related complications, and AIDS-related neurological diseases.

Gilead Sciences, Inc., was the second-leading funder, with an estimated investment of $573 million. In 2009, Gilead had two phase III (for FTC/TDF/rilpivirine and elvitegravir) and two phase II (for fixed-dose combinations with elvitegravir/cobicistat/FTC/TDDF or Quad) trials underway for the treatment of HIV along with several experimental treatments for cardiovascular, liver, and respiratory disease (Gilead Sciences, Inc. 2010b). According to Gilead, a total of $831 million was spent on R&D in 2009. Regrettably, investment data by therapeutic area was not provided. To generate the $573 million estimate, TAG reviewed Gilead's clinical research pipeline and Form 10-K to determine how much revenue was raised from ARV sales. With HIV medicines generating $4.87 billion or 69% of the company's total revenue, TAG calculated that HIV drug development costs could be estimated at 69% or $573 million of total R&D expenses for 2009 (Gilead Sciences, Inc. 2010a).

Though TAG was only able to secure funding data from seven companies, we are aware industry investments in HIV drug discovery and development is much greater, based on clinical trial activity in 2009. This is discussed further in this report.

FIGURE 6

Drug Discovery and Development: 2009 Investments

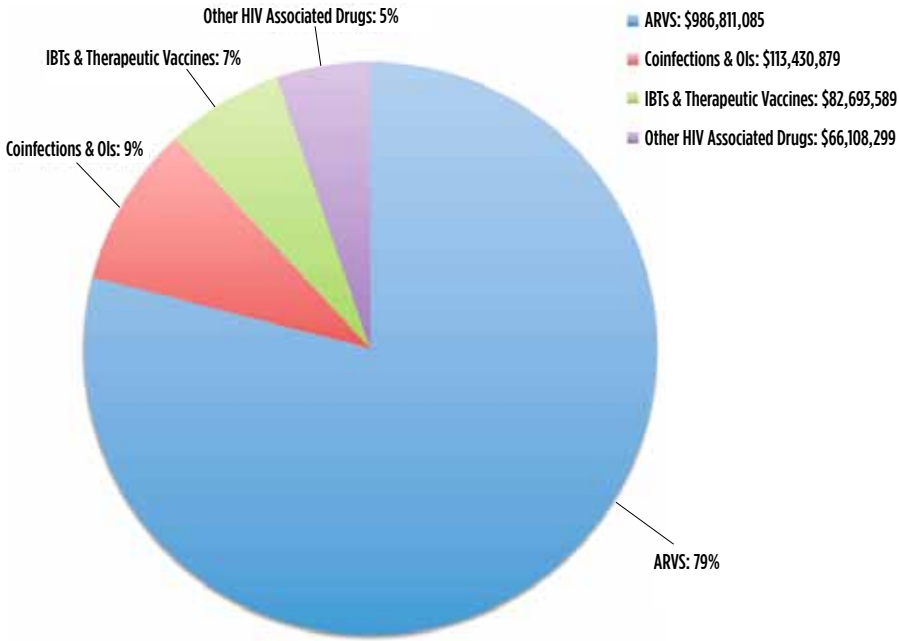


#	Funding Institution	Total (USD)	#	Funding Institution	Total (USD)
1	US NIH	$599,875,000	16	Company B	$1,231,295
2	Gilead Sciences	$573,390,000	17	BMGF	$790,723
3	EC	$16,870,320	18	Cytheris	$619,744
4	UK MRC	$11,486,236	19	Victorian Dept. of Human Services	$546,319
5	Company A	$8,000,000	20	Brazil MoH	$469,243
6	ANRS	$6,543,535	21	Bettancourt Schueller Foundation	$352,128
7	EDCTP	$5,845,440	22	Italy MoFA	$333,333
8	CIHR	$3,889,946	23	USAID	$304,449
9	Wellcome Trust	$3,360,148	24	IPST	$265,072
10	SEEK	$3,313,100	25	ICMR	$264,019
11	GeoVax Labs	$3,045,823	26	amfAR	$236,650
12	Japan MoH	$3,044,415	27	BELSPO	$102,910
13	Australia NHMRC	$1,870,835	28	Australian Research Council	$97,137
14	Italian MoH	$1,466,663	29	CANFAR	$68,485
15	Esteve	$1,290,000	30	FHI	$38,655
			31	New Zealand HRC	$32,230
				Grand Total	**$1,249,043,852**

Drug discovery and development areas for treating HIV infection and its consequences include ARV drug development, drug development to treat coinfections and OIs, IBTs such as anti-inflammatory drugs and therapeutic vaccines, and other HIV-associated drugs to treat AIDS-related cancers and neurological disorders. In 2009, ARV drug development was the most-funded therapeutic research area, receiving $987 million (76%).

FIGURE 7

Drug Discovery and Development Investment Areas



2.7 Antiretroviral Therapy Prevention

ART prevention is an approach that deploys ART to prevent new infections. Approaches include the prevention of vertical transmission, first discovered with the drug AZT in 1993 (ACTG 076); PEP; ART-based microbicides, such as the July 2010 breakthrough study CAPRISA-004, which found that 1% TDF gel applied twice daily reduced HIV acquisition in HIV negative women by 39%; and PrEP, recently validated as a prevention approach by the November 2010 iPrEX trial results, which found that once-daily oral Truvada (TDF/FTC) reduced HIV acquisition by 44% in HIV negative men who have sex with men and in transgender persons.

Most recently, the NIH-funded HPTN 052 study taking place in Botswana, Brazil, India, Kenya, Malawi, South Africa, the United States, and Zimbabwe examined the effect of immediate treatment at enrollment with CD4 counts between 350 and 550/mm^3, versus delaying ART until CD4 counts dropped below 250, among 1,763 serodiscordant couples. Results from the study—scheduled to continue until 2015—were released early by the Data and Safety Monitoring Board, and randomization was ended due to a massive 96% reduction in interpartner HIV infection rates (HIV Prevention Trials Network/National Institutes of Health 2011; National Institute of Allergy and Infectious Diseases, National Institutes of Health 2011). The study also found a statistically significant drop in extrapulmonary TB cases among those on early therapy.

A more recent study, HPTN 065, is evaluating whether health-facility-level HIV testing and linkage to care can increase HIV treatment uptake, enhance treatment success, and reduce new HIV infections in the Bronx, New York, and Washington, D.C.

Research investments in ART prevention for 2009 by the NIH and the Canadian Institutes of Health Research–HIV/AIDS Research Initiative (CIHR) were $84.9 million. The NIH invested $84.8 million investigating approaches to interrupt vertical transmission ($57.5 million), and approaches to prevent horizontal transmission ($27.3 million), which investigate PEP, PrEP, and the effect of ART treatment on transmission in discordant couples and on community-wide viral load. The CIHR invested $112,000 across three studies to evaluate the expansion of ARV access and reduction of HIV transmission among specific populations.[4]

The ART prevention paradigm has the potential to integrate prevention and treatment service delivery, improve program cohesion, and save billions of dollars and—more important—millions of lives while putting the epidemic in reverse for the first time, helping to pave the way for its elimination.

2.8 Operational and Implementation Science

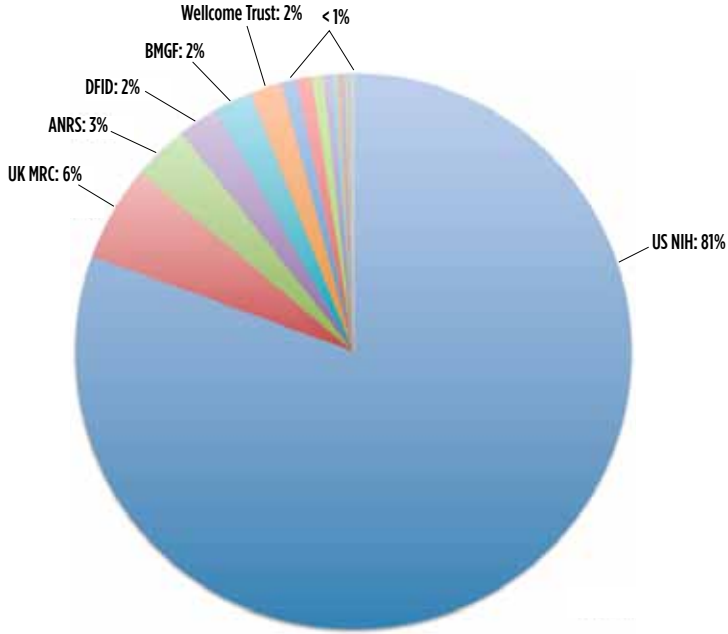
Funding in 2009 to support operational and implementation science related to HIV treatment totaled $308 million. Research funded by the NIH ($248 million), the UK Medical Research Council (UK MRC; $17 million), and the Agence Nationale de Recherche sur le SIDA (ANRS; $10 million) supported a range of projects from epidemiological surveillance to evaluation of treatments, AIDS-related comorbidities, and other therapeutic interventions.

While much more implementation science is taking place around the world, funded by host countries and by bilateral and multilateral donors such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria; the U.S. President's Emergency Plan for AIDS Relief, and USAID,[5] program funds are not always clearly reported or tracked.

4. ART prevention research being supported by other funders was not reported to TAG by press time. Funding levels for many of these interventions in 2009 are discussed more fully in HIV Vaccines and Microbicides RTWG 2009.
5. These donors did not report 2009 treatment related operational or implementation science projects to TAG.

FIGURE 8

Operational and Implementation Science: 2009 Investments



#	Funding Institution	Total (USD)	#	Funding Institution	Total (USD)
1	US NIH	$247,914,000	14	EDTCP	$318,676
2	UK MRC	$17,203,837	15	ICMR	$290,964
3	ANRS	$9,897,442	16	AALA/Life Ball	$277,859
4	DFID	$7,247,497	17	Australian Research Council	$276,793
5	BMGF	$6,793,537	18	Research Foundation Flanders	$274,810
6	Wellcome Trust	$5,747,211	19	SRC	$217,553
7	EC	$2,745,725	20	WHO	$39,720
8	CIHR	$2,743,296	21	India NACO	$36,510
9	Japan MoH	$2,049,313	22	Flemish Government	$31,691
10	Australia NHMRC	$1,448,812	23	Amsterdam School for Social Science Research	$28,189
11	Brazil MoH	$763,590	24	Papua New Guinea IMRF	$22,056
12	amfAR	$671,811	25	Centrum voor Informatie en	$8,451
13	DGIS	$653,238		Samenlevingsopbouw VZW	
				Grand Total	**$307,702,581**

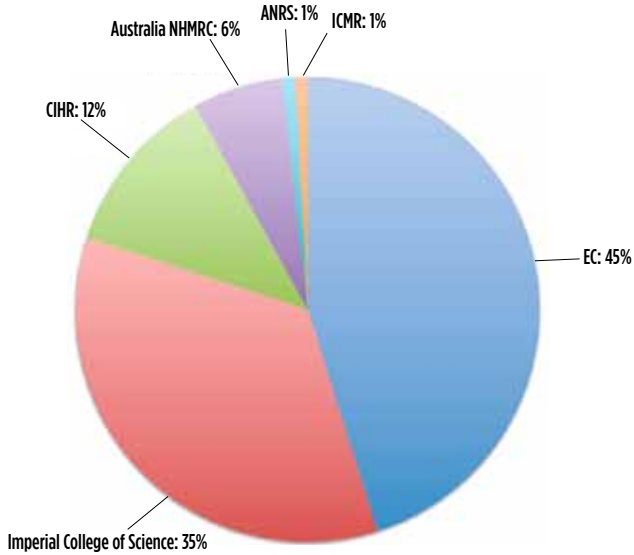
2.9 Diagnostics

Though TAG did not originally intend to collect funding data on HIV/AIDS diagnostics research, six funders reported spending a small portion of their HIV funding on such research. Since the initiation, delivery, and monitoring of ARV therapy is based on CD4 counts and HIV RNA levels, and because simpler monitoring tools are included in the Treatment 2.0 framework, TAG included diagnostics as an HIV treatment-related research area.[6]

In 2009, the European Commission (EC) invested $951,336 (45%) on the DETECTHIV project, a three-year study to develop a sensitive nanoparticle assay for the detection of HIV. The Imperial College London awarded $753,358 (35%) to the Macfarlane Burnet Institute for Medical Research and Public Health to develop point of care tests for CD4 T cells.

FIGURE 9

Diagnostics: 2009 Investments



#	Funding Institution	Total (USD)
1	EC	$951,336
2	Imperial College of Science	$735,358
3	CIHR	$252,351
4	Australia NHMRC	$132,121
5	ANRS	$19,473
6	ICMR	$17,375
	Grand Total	**$2,108,014**

6. TAG recognizes that diagnostics funding is underreported (e.g., the NIH supports diagnostics research but that is not reflected here because data could not be disaggregated). We will improve the accuracy of these data in future reports by including diagnostics as a research category.

2.10 Private-Sector Clinical Research Activity in 2009

Of the 144 institutions surveyed by TAG, 46 were private-sector funders from the pharmaceutical and biotechnology industries. Seven companies shared 2009 HIV treatment R&D investments; 3 companies confirmed no longer funding HIV treatment R&D; 1 declined to participate; and the remaining 35 private-sector funders did not respond to the survey.

Due to the difficulty of securing private-sector investments, TAG conducted an online search of clinical research activity sponsored or cosponsored by the private sector in 2009. Using company websites, annual reports, and information posted on the Clinical Trials Registry (http://clinicaltrials.gov), TAG identified 20 private-sector companies supporting ARV clinical trial activities (see Table 5) and 19 companies sponsoring trials on immune-based therapies and therapeutic vaccines (see Table 6). The results of this desktop research find substantial private-sector involvement in HIV therapeutics, despite recent concerns about shrinking pipelines (Cortez 2011).

In 2009, at least four nucleoside or nucleotide reverse transcriptase inhibitors were in clinical development, along with at least four non-nucleoside reverse-transcriptase inhibitors (NNRTIs), two protease inhibitors, three integrase inhibitors, six CCR5 receptor blockers, three pharmacokinetic enhancers, and two FDCs (see Table 5), plus a broad range of potential therapeutic vaccines and immune-based therapies (see Table 6).

Postmarketing research also continues on recently approved drugs, and in the worldwide generic sector potential FDCs are not as limited by intellectual property restrictions as are potential brand-name combinations in industrialized countries.

In addition to compounds already in clinical trials, several large- and many medium-sized and smaller players in the biopharmaceutical sector continue to explore novel and innovative approaches to HIV therapy, including new molecular targets as well as extended, long-acting compounds that could be taken, perhaps by injection, once or twice a month or even less often. Finally, there is increasing interest among both the public and private sector in research to lead to a functional (drug-free remission) or sterilizing (elimination of all HIV nucleic acids and virions from the body) cure for HIV infection.

TABLE 5

Overview of ARV Clinical Trial Activity Sponsored by the Private Sector in 2009

SPONSOR	PHASE I	PHASE II		PHASE III	PHASE IV
		PHASE IIA	PHASE IIB		
Achillion Pharmaceuticals		elvucitabine (NRTI)			
Ardea Biosciences		RDEA806 (NNRTI)			
Avexa		AVX-201 apricitabine			
Boehringer Ingelheim Pharmaceuticals					NEwArT
Bristol Myers Squibb		BMS-663068 (HIV attachment inhibitor BMS-626529)			
Chimerix	CMX157				
Gilead Sciences				cobicistat (pl coenhancer)	
				elvitegravir (intergrase inhibitor)	
				elvitegravir/emtricitabine/ tenofovir disoproil fumurate/cobicistat (FDC)	
GSK	CTP-518 (PI)				
Hoffmann-La Roche/Trimeris					AMICI
Merck		Isentress (raltegravir) vs efavirenz			
Peregrine Pharmaceuticals	bavituximab				
Pfizer/ViiV	PF-3716539				
Progenics Pharmaceuticals		PRO-140 (CCR5 antagonist)			
RFS Pharma		amdoxovir (DAPD)			
Shionogi & ViiV Healthcare		SINGLE (GSK1349572)			
TaiMed Biologicals		ibalizumab (TMB-355)			
Tibotec Pharmaceuticals				rilpivirine (TMC278) (NNRTI)	
	TMC558445				
	TMC310911				
Tobira Therapeutics	TB 220 (CCR5)				
		TBR-652 (CCR5 antagonist)			
ViiV Healthcare		2248761 (IDX-899) (NNRTI)			
		PF-232798 (CCR5 antagonist)			
		UK-453061 (NNRTI)			
		1349572			
		S/GSK 1265744			
					Maraviroc in children & adolescents
Abbott/BMS/Gilead/GSK/ Merck/Tibotec & other public sector funders					START

TABLE 6

Overview of Immune-based Therapies and Therapeutic Vaccine Clinical Trial Activity Sponsored by the Private Sector in 2009

SPONSOR	PHASE I	PHASE II		PHASE III	PHASE IV
		PHASE IIA	PHASE IIB		
Argos Therapeutics		AGS-004			
Bavarian Nordic	MVA-mBN120B				
Bionor Pharma		vacc-4x			
Cobra Pharmaceuticals/ Impfstoffwerk Dessau-Tornau/ University of Oxford/UK MRC		DNA/MVA			
Cytheris		INSPIRE (CLI 107-06)			
		INSPIRE 2 (CLI-107-13)			
		INSPIRE 3 (CLI-107-14)			
Enzo Biochem		StealthVector HGTV43T			
EUFETS AG	M87o				
FIT-Biotech		FIT-06, GTU-MultiHIV Vaccine			
Genetic Immunity		DermaVir (LC002)			
GlaxoSmithKline	HIV Vaccine 732462				
Hoffmann-La Roche/NIAID		Pegasys (peginterferon alfa-2a)			
Johnson & Johnson		OZ1 ribozyme gene therapy			
SEEK	HIV-v				
Pfizer					Maraviroc (Selzentry)
Salix Pharmaceuticals/ University of California-San Francisco					Mesalamine (5-aminosalicylic acid)
Sangamo Biosciences/ University of Pennsylvania		Zinc Finger Nucleases SB-728-T			
Sanofi Pasteur	Tat Vaccine				
Tarix Pharmaceuticals	TXA127				
VIRxSYS		VRX496			

2.11 Discussion

From early reports in the United States to the most recent data from China, highly effective antiretroviral therapy (HAART) reduces mortality among those with advanced HIV infection by over two-thirds (Pallela et al. 1998; Zhang et al. 2011). Its rapid uptake brought AIDS death rates down dramatically—first in the developed and now in developing countries. New and emerging data (Abdool Karim et al. 2010; Grant et al. 2010; HPTN/NIAID 2011) indicate the further potential of ART prevention to dramatically reduce HIV transmission.

This report finds that public, private, and philanthropic research funders invested at least $2.46 billion US dollars in HIV treatment–related research in 2009. Given that the private sector was generally unresponsive to the survey request, TAG believes the true figure is likely to be at least $1.2 billion higher, as the substantial drug development activity shown in Tables 5 and 6 indicates that many sponsors besides the seven, which reported their investments to TAG in 2009, are involved in expensive clinical trials activities. Preclinical activity is mostly unquantified, as this often is not yet reported in the scientific literature due to the preliminary nature of the research and, often, the limitations of patent or intellectual property concerns.

One recent market analysis estimated that "the global market for HIV treatments was valued at over US$13 billion in 2009 with the U.S. being the largest market and the five major [European Union] markets collectively being the second largest market". The report also states there are approximately 297 compounds in development, with Gilead Sciences leading "the HIV market with a market share of approximately 40%" (Market Research News 2011).

The challenge with developing an R&D estimate is that there are too many "unknowns" and no willingness from industry to disclose data and put an end to the guessing game. Nevertheless, efforts have been made to quantify R&D costs. A 2003 article from DiMasi and colleagues estimated the average out-of-pocket costs of discovering and developing a single new drug to be $403 million (in year 2000 dollars) based on a sample of ten pharmaceutical companies whose names and drugs remained anonymous in the study (DiMasi et al. 2003). This often cited article offers insight into the costs and processes involved in drug development but fails to provide enough evidence to corroborate the full figure, which includes alleged cost of capital and rises from the out-of-pocket cost to $802 million. A 2011 study published by Light and Warbuton, by contrast, disputes the DiMasi study findings and produces a median estimate of $43.3 million per new drug (Light & Warbuton 2011), which TAG predicts is far too low given that a phase II tuberculosis drug trial cost $52.8 million in 2009 alone (TAG 2011). The two studies have stirred heated debate, but they prove that without full disclosure of R&D investments, estimating drug development costs is a futile endeavor.

Finally, a recent resource-tracking project carried out by Policy Cures in 2010 reported that of the $1.4 billion invested in HIV treatment and prevention R&D in 2009, the private sector invested 3.1% of the funding total or $43.4 million (Policy Cures 2011). The study covered basic science, drugs for developing country needs, preventive vaccines, diagnostics, and

microbicides. For investments in HIV drugs for developing countries, only funding for FDCs and pediatric formulations were tracked, omitting R&D funding in developed countries, research on treatment for adults, and operational and implementation science, which can amount to several more hundreds of millions—if not billions in untracked funding data for HIV treatment R&D.

This report, which marks the beginning of an ongoing effort to annually monitor worldwide investments in HIV treatment research, will seek to get direct industry reports of out-of-pocket costs and will not adjust for cost of capital.

3. Conclusion and Recommendations

3.1 Conclusions

> *Radical simplification, innovation in drug design and diagnostics, renewed commitment and resources, and adapted delivery systems will be crucial to reach universal and sustainable coverage of* [antiretroviral] *treatment for those in need.*
>
> —Gottfried Hirnschall and Bernhard Schwartländer, "Treatment 2.0: Catalysing the Next Phase of Scale-up," *Lancet* 2011.

This report is a first step toward establishing a baseline of R&D investments in developing new or enhancing existing HIV therapeutic regimens. TAG solicited information from 144 funding institutions and gathered disbursement data from 48 funders to generate a $2.5 billion investment in HIV treatment R&D for 2009.

Public-sector funders by far made the largest investments to HIV treatment R&D—$1.8 billion (75%)—in 2009. Data collected from seven private-sector companies generated a low investment figure of just $591 million—making it difficult to report an accurate industry total. Multilateral agencies invested $39 million, and philanthropic foundations invested $31 million.

Of the $2.5 billion reported global investment, half ($1.2 billion) went toward research to develop new and optimize existing compounds to treat HIV infection and its related comorbidities. Basic science research that explores HIV virology, immunology, and pathogenesis received $787 million in 2009. Operational and implementation science that evaluates new or existing interventions within routine program settings, including epidemiological and surveillance studies, received $308 million. Of the remaining funds, $85 million went toward ART prevention research, $31 million to applied/infrastructure/unspecified research, and $2 million to diagnostics research.

Despite a low response rate from the private sector, TAG found at least 20 companies supporting ARV clinical trial activities and 19 companies sponsoring immune-based therapies and therapeutic vaccines trials, which amount to millions of dollars per trial. The costs are far greater in late stage clinical trials such as Gilead's QUAD (elvitegravir/cobicistat/FTC/TDF) and Tibotec's Edurant (rilpivirine a new NNRTI), both approved as recently as May 2011 (FDA 2011).

TAG identified $2.5 billion in funding for HIV treatment R&D in 2009—investments that were overwhelmingly supported by U.S.-based institutions. TAG believes that middle-income countries such as China, Mexico, the Russian Federation, and South Africa, among others, are investing in HIV treatment R&D, but such investments were not captured in this report.

With ongoing budget battles in the United States and threats of slashing NIH funding back to 2008 fiscal year levels (amfAR 2010), the HIV therapeutics field urgently needs more diverse funding streams, including increased funding from high- and middle-income countries as well as the private sector. The biopharmaceutical industry is a critical partner in HIV treatment research and its leaders should not shy from reporting their investments in mitigating and ending the epidemic.

TAG believes at least six emerging trends will define the future of HIV treatment related research over the coming decade:

1. Earlier use of HIV treatment will become more widespread as the population of those at greatest need—first, those with clinical AIDS or CD4 counts below 200/mm^3, and then those with CD4 counts below 350/mm^3, along with those who are pregnant, have active TB disease, or are infected with HBV at any CD4 cell level—receive therapy.

2. Increasing use of HIV treatment therapy will be complemented by its expansion into newer uses for treatment-and-prevention—as in the serodiscordant couple study findings announced recently (HPTN/NIAID 2011), as well as treatment-for-prevention approaches such as oral PrEP (Grant et al. 2010) and vaginal microbicides (Abdool-Karim et al. 2010) are further validated and rolled out.

3. The trend for simpler, easier-to-take, more forgiving, less toxic, treatment regimens such as once-daily FDCs—and later, perhaps, even longer-acting injectable combinations—will continue to drive both innovation and generic formulations.

4. A wave of imminent patent expirations for earlier-approved ARV therapies around 2015 will drive new generic combination approaches, and will continue to drive down costs (Clinton Health Access Initiative et al. 2011).

5. New drugs in existing classes and new classes of drugs will continue to be developed, potentially enabling further simplification and decentralization of HIV treatment.

6. All of these trends indicate the need for HIV therapy—and for innovative, simpler, more robust treatment regimens—will continue to grow over the coming decade.

The HIV treatment research landscape is changing. Thanks to recent treatment scale-up and prevention science breakthroughs and the new global treatment target of 15 million by 2015 (UNGASS 2011), there is real momentum to bring the epidemic under control and ultimately end it. To capitalize on these scientific gains continued investment and innovation are necessary to prevent new infections, to ensure people currently on treatment are able to continue, and to scale up treatment to reach all those who will benefit from earlier initiation of ART.

3.2 Recommendations

1. Continued support for basic research, drug discovery and development, and operational and implementation science from the public sector is essential to move forward the HIV prevention revolution, Treatment 2.0, and to turn the epidemic in reverse and ultimately eliminate it.

2. The private sector continues to play an essential role in HIV drug discovery and development. Companies should not shy away from revealing their research investments; transparency will help to bring the pandemic under control and to end it. Innovator companies should explore new models to more rapidly bring new drugs and combinations to developing country settings through new mechanisms such as the Medicines Patent Pool, and should partner with public sector and philanthropic initiatives to speed the development of pediatric ART regimens, which regrettably lag behind adult treatment by a decade or more in some cases.

3. Bilateral and multilateral donors and host countries need to significantly increase the transparency of their investments in operational and implementation science to validate the most effective ways of using HIV treatments and ART prevention together in programmatic settings.

4. Emerging economies—such as Brazil, China, India, Russia, South Africa, and Thailand, among others—have the potential to play a much more productive role in HIV treatment related research and should invest significantly in product discovery and development in order to address the health needs of their own populations and assist in their economic development.

5. New and simplified diagnostic tests, including point-of-care dipsticks for early infant HIV diagnosis, acute primary infection diagnosis, semiquantitative or quantitative HIV RNA and CD4 count measurements will greatly assist in the proper diagnosis, treatment initiation, staging, and monitoring of adherence and response to therapy. Investment in these areas is anemic and must be substantially increased by all stakeholders.

6. Donors and countries must commit to meeting their Abuja, UN Millennial Development Goals, Monterrey, and Universal Access commitments so that sufficient resources are available to meet the growing health needs of the global population, including those at risk for and those infected by HIV.

7. The HIV pandemic is a long-wave pandemic. Activists, implementers, industry, policy makers, providers, and scientists must plan to invest smartly and quickly now so as to bring AIDS under control as quickly as possible and to set the stage for its elimination.

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Appendix A: Acronyms

ART — antiretroviral therapy
ARV — antiretroviral
CIHR—Canadian Institutes of Health Research–HIV/AIDS Research Initiative
FDCs — fixed-dose combinations
HBV — hepatitis B virus
HCV — hepatitis C virus
HIV — human immunodeficiency virus
IBTs — immune-based therapies
NIH — U.S. National Institutes of Health
NNRTIs — nonnucleoside reverse-transcriptase inhibitors
OAR—NIH Office of AIDS Research
OIs — opportunistic infections
PEP — postexposure prophylaxis
PrEP — preexposure prophylaxis
R&D — research and development
RTWG—Resource Tracking Working Group
TAG — Treatment Action Group
TB — tuberculosis
WHO — World Health Organization

APPENDIX B: 2009 HIV R&D NONRESPONDENTS

#	Funding Institution	Funder Type
1	Aaron Diamond AIDS Research Center	P
2	Abbott Laboratories	C
3	Achillion Pharmaceuticals	C
4	Ardea Biosciences	C
5	Argos Therapeutics	C
6	Aurobindo Pharma	C
7	Australian Department of Health and Age (CDHA)	P
8	Avexa	C
9	Bavarian Nordic	C
10	Becton Dickinson & Company (BD)	C
11	Bionor Pharma AS	C
12	Boehringer Ingelheim Pharmaceuticals	C
13	Brazilian Innovation Agency (FINEP)	P
14	Bristol-Myers Squibb	C
15	Chimerix	C
16	China National Center for Disease Control & Prevention/National Vaccine & Serum Institute	P
17	Chinese Ministry of Science and Technology	P
18	Combino Pharm	C
19	Danish Ministry of Foreign Affairs	P
20	Department of Health, South Africa	P
21	Department of Science & Technology, South Africa	P
22	Development Cooperation Ireland (DCI)	P-D
23	Enzio Biochem	C
24	EUFETS-AG	C
25	FIT-Biotech	C
26	French Development Agency, Agence Francaise de Develoment (AFD)	P
27	Genetic Immunity	C
28	German Research Foundation (DFG)	P
29	GlaxoSmithKline	C
30	Global Fund	M
31	Hoffmann-La Roche	C
32	IAS	M
33	Idenix Pharmaceuticals	C
34	Imquest Life Sciences	C
35	Indian Council of Medical Research—National Institute for Research in Reproductive Health	P
36	Indian Department of Science & Technology	P
37	Infectious Disease Research Institute (IDRI)	P
38	Inovio	C
39	Inserm—Institute of Infectious Diseases	P
40	Japan International Cooperation Agency	P
41	Japan National Institute for Infectious Diseases	P
42	Johnson & Johnson	C

P = Public Sector Agency **P-D** = Public Sector Development Agency
F = Foundation/philanthropy **C** = Corporate/private sector
M = Multilateral Agency

43	Karolinska Institute	P
44	Matrix Laboratories Limited	C
45	Max Planck Institute	P
46	Medical Research Council of the Finnish Academy	P
47	Mexican National Institute of Public Health (INSP)	P
48	Ministry of Foreign Affairs, France	P
49	Moriah Fund	F
50	Office of Global AIDS Coordinator (OGAC)	P
51	OPEC Fund for International Development	P-D
52	Overbrook Foundation	F
53	Peregrine Pharmaceuticals	C
54	Progenics	C
55	Public Health Agency of Canada	P
56	Ranbaxy	C
57	Research Council of Norway	P
58	Rockefeller Foundation	F
59	Royal Norwegian Ministry of Foreign Affiars (RMFA)	P
60	Salix Pharmaceuticals	C
61	Sangamo Biosciences	C
62	Sanofi Pasteur	C
63	Shionogi Co., Ltd	C
64	South Africa Department of Science and Technology (DST)	P
65	South Africa Medical Research Council (MRC)	P
66	Starr Foundation	F
67	Swedish International Development Agency (SIDA)	P
68	TaiMed	C
69	Tarix Pharmaceuticals	C
70	Thailand—Department of Disease Control, Ministry of Public Health (MOPH)	P
71	Tides Foundation/John Lee Fund	P
72	UK Biotechnology and Biological Sciences Research Council (BBSRC)	P
73	Until There Is a Cure Foundation	F
74	US Department of Defense (DoD)	P
75	US Department of Defense (DoD): Defense Advanced Research Projects Agency (DARPA)	P
76	US Food & Drug Administration (FDA)	P
77	USAID	P-D
78	Veterans Affairs	P
79	Virostatics	C
80	VIRxSYS Corporation	C
81	Walter Reed	P
82	World Bank	M
83	World Health Organization: Special Programme for Research & Training in Tropical Diseases	M

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