amfAR
MAKING AIDS HISTORY

In Memoriam
Dame Elizabeth Taylor
Founding International Chairman

In Memoriam
Mathilde Krim, Ph.D.
Founding Chairman

2019 Action Plan

After more than three decades of combating HIV, the world stands on the threshold of an important decision. Will we muster the will, resources, and ingenuity to end the AIDS epidemic, or will we continue to struggle against new infections and the ever-mounting cost of treating them? As always, amfAR believes that an end to AIDS is within reach. We intend to continue our vigorous pursuit of this goal by using our unparalleled expertise to define the global cure research agenda, identify the research studies best able to propel the field forward, and promote policies that strengthen front-line efforts to help people living with the virus.

Progress on the research front continues to generate tremendous momentum. Scores of amfAR-funded studies are helping to overcome the most complex remaining barriers to a cure, increasing our ability to locate, awaken, and—one day—eradicate hidden viral reservoirs in the body. In one of our most promising investigations, amfAR-funded scientists on two continents are at work on a never-before-tried application of gene therapy.

This **Action Plan** provides an overview of amfAR's research goals and objectives for 2019. It also describes how we will use our advocacy skills to reduce the spread of HIV among populations at greatest risk.

In this penultimate year of our **Countdown to a Cure for AIDS** initiative, amfAR will continue our unwavering efforts to quell the epidemic's most persistent threats and work toward the cure that is increasingly within our reach.

We'll do this by investing in the most innovative new scientific ideas and fighting for policies that protect those living with and at risk of HIV. As we embark on another exciting year of work, we are mindful of the pioneers whose inspiration and determination sparked this movement more than thirty years ago—and grateful to all the donors whose generosity is helping us **MAKE AIDS HISTORY**.

amfAR's Countdown to a Cure for AIDS awards multi-year grants to scientists working on studies related to the four key remaining challenges to curing HIV. Each challenge pertains to hidden reservoirs of HIV that persist—even in individuals on antiretroviral therapy (ART)—and are the major obstacle to eradicating the virus. These challenges are:

Chart the precise locations of viral reservoirs;

Understand how HIV persists in the reservoirs;

Record how much virus is in the reservoirs;

Eliminate the reservoirs of infected cells.

GOAL 1:
Remain at the Forefront of HIV Cure Research

amfAR does more than invest in the world's most innovative cure research. We use our three decades of expertise and leadership to help define the global HIV cure research agenda. To ensure we fund the studies most likely to answer the remaining questions standing between us and a cure, our Research staff and Program Advisory Council regularly evaluate the current state of cure research and determine the most promising avenues for future investigations.

Our targeted investment strategy yields impressive results. While amfAR grants comprise 2% of the total global investment in cure research (making us the world's fourth-largest HIV cure funder), our studies yield a remarkable 20% of HIV cure papers published in scientific journals—a testament to the wealth of new knowledge and insight our strategy produces.

Promising studies underway in 2019 include a novel application of gene therapy that uses three methods simultaneously to attack the major barrier to a cure, and the next phase of the world's largest study of the role stem cell transplants may play in an HIV cure.

Research Highlight:
Gene Therapy and ARCHE-GT

There is consensus among the scientific community that **gene therapy** is one of the most promising approaches to an HIV cure. But there is also concern that its complexity may limit its potential to be used on a broad scale for all 37 million people living with HIV.

amfAR has taken on this scalability challenge by designing an ambitious and collaborative study known as **ARCHE-GT**.

Gene therapy offers the tantalizing possibility of manipulating DNA as a means of attacking infected cells that make up the HIV reservoir, altering the susceptibility of cells to HIV infection, or enhancing the ability of the immune system to attack or block the virus. But it carries a number of risks and challenges. Scientists need to find ways to improve the efficiency of appropriately altering DNA, effectively target the correct cells, and enable the therapy to safely persist long enough to have an effect.

Through ARCHE-GT, amfAR has forged a unique collaboration among world leaders in gene therapy that began with a think tank in 2016. The amfAR-led meeting gave rise to a plan to create the first combination intervention that will simultaneously address the main barrier to a cure, the viral reservoir. In a three-pronged attack on the HIV reservoir, the researchers will employ broadly neutralizing antibodies, CAR stem cells—cells genetically reprogrammed to recognize and attack disease cells—and molecular scissors targeting the virus inside the cell.

The goal is to 1) induce CAR stem cells to kill HIV-infected cells; 2) express two different antibodies that simultaneously neutralize virions (virus that exists outside of cells) in the blood and tissues and kill HIV-infected cells, and; 3) use an enzyme (Brec1) that removes the provirus (virus that has been integrated into a cell's DNA).

ARCHE-GT is one of the most exciting and far-reaching HIV cure research efforts underway anywhere. By combining three of the most powerful gene therapy tools in one intervention, the researchers are hoping to attack HIV wherever it appears in the body, increasing their chances of eliminating it altogether. This study also has the potential to revolutionize the broader field of gene therapy, by pitting these various approaches against each other to see which is most effective. We are proud to partner with talented and innovative scientists at seven research institutions for this study, which holds great promise for developing the scientific basis of a cure.

Research Highlight:
Stem Cell Transplants and ICISTEM

amfAR funded the study that confirmed that Timothy Brown, "the Berlin Patient," had become the first—and still only—person known to be cured of HIV. Brown, who also had lymphoma, was cured

after receiving a stem cell transplant in 2007 from a donor with a rare genetic mutation—CCR5-delta32—that confers resistance to the virus. In the years since, it has been unclear whether that cure can be replicated. In 2012, amfAR began discussions with—and later funded—a group of researchers who established an international research consortium, now known as **ICISTEM** (icistem.org), to answer that question.

ICISTEM includes HIV cure researchers, cancer transplant doctors, and doctors working to register stem cell donors and test their cells for the genetic mutation. It remains the world's largest study to date on the role of stem cell transplants in HIV cure. The team has enrolled a cohort of more than 38 patients with cancer and HIV who have received or soon will receive transplants of stem cells with the CCR5-delta32 mutation. ICISTEM has also identified over two million potential stem cell donors with the mutation.

ICISTEM researchers have conducted exhaustive testing for persistent HIV reservoir in transplant recipients. In several cases, they were unable to find evidence that any HIV remains—an encouraging sign. In 2019, the team will embark on the next phase of this scientific journey—and the definitive test of a cure for these patients—the withdrawal of antiretroviral therapy.

This strategic interruption of treatment will include an immune intervention with two HIV-specific neutralizing antibodies, to maximize the chance of achieving a cure. During that phase, researchers will track patients' immune responses to better understand the mechanisms by which a stem cell transplant-based cure may be achieved. That could provide insights critical to the development of a more broadly applicable cure.

Research Highlight:
The amfAR Institute for HIV Cure Research

The **amfAR Institute for HIV Cure Research**, headquartered at the University of California, San Francisco, was launched in 2016 with a five-year, $20 million grant. Its teams work in close collaboration with Dr. Rowena Johnston, amfAR vice president and director of research, as well as several other research institutions in the region. Thanks to the considerable progress the Institute has made in achieving our C-U-R-E roadmap goals, it is now centering its efforts on a clinical trial of a promising strategy known as "shock and kill," led by Dr. Steven Deeks.

This multi-pronged study will enroll 20 patients living with HIV and test a combination curative therapy that includes three vaccines, two broadly neutralizing antibodies, and an immunotherapy drug called MGN1703, which activates the immune system. Together, these agents have the potential to enhance the immune system's capacity to kill HIV-infected cells.

Research Highlight:
Other Notable Studies Underway in 2019

In 2019, we will continue funding both the new and ongoing studies most likely to answer the vital questions that can dismantle the barriers to a cure. This includes ensuring a future cure works for all populations affected by the virus. Although the vast majority of HIV-infected individuals live in low- and middle-income countries, few cure studies are currently done in these nations, due to a lack of funding. Therefore, a 2019 priority is working with researchers in these settings. Highlights of these current amfAR-funded studies include:

- **Dr. Godwin Nchinda of the Chantal Biya International Reference Center for Research on the Prevention and Management of HIV/AIDS in Yaounde, Cameroon**, is studying a cohort of women who received ART during pregnancy and continue to control the virus after halting ART after giving birth. This study could identify novel ways of bringing about ART-free viral control.
- **Dr. Reena Rajasuriar of the University of Malaya in Kuala Lumpur, Malaysia**, is testing whether frequent exposure to pathogens commonly encountered by people living in low-income countries expands the HIV reservoir differently compared to those in high-income countries, where exposure to these pathogens is less frequent. Dr. Rajasuriar's work is bringing us closer to understanding whether different curative interventions may be required in lower- versus higher-income settings.
- **Dr. Alex Sigal of the African Health Research Institute in Durban, South Africa**, is investigating how tuberculosis (TB), a common co-infection in people living with HIV in low- and middle-income countries, impacts the HIV reservoir. His discoveries could help ensure that a future cure works in the large percentage of individuals co-infected with HIV and TB.

Disseminating Our Results

Disseminating our findings will remain an important part of amfAR's research mission. Many of our researchers have been invited to give presentations at prestigious scientific conferences, including the annual Conference on Retroviruses and Opportunistic Infections (CROI), the Keystone Symposium on HIV Persistence: Pathogenesis and Eradication, and the 10th International AIDS Society Conference on HIV Science, among others. We anticipate that dozens of them will publish research papers in major scientific journals.

As a thought leader in HIV cure research, amfAR will convene think tanks for leading scientists in HIV and relevant fields to discuss innovative strategies for overcoming the most stubborn challenges in cure research. Our Research staff will incorporate findings from these discussions into the design of studies for our Countdown to a Cure initiative. And we continue to assert our leadership in cure research by publishing scientific papers authored by amfAR staff, presenting our work at conferences, and providing interpretation and contextualization of research findings for the media.

amfAR will be a major presence at key conferences and symposia throughout 2019, including:

CROI: March 4-7
10th IAS Conference on HIV Science
Mexico City • July 21-24

Cure Summit, amfAR Institute for HIV Cure Research
San Francisco • November 21

The amfAR Institute will also host cure-related symposia throughout the year, including our annual World AIDS Day Cure Summit. These gatherings provide invaluable opportunities for amfAR to engage researchers and the larger HIV community.

GOAL 2:
Reduce the Harmful Impact of HIV/AIDS Through Public Policy

amfAR's Public Policy Office (PPO), based in Washington, D.C., is dedicated to advocating policies that protect the rights and health of people living with HIV in the U.S. and around the world.

Domestic Advocacy

In the U.S., where HIV is mainly concentrated within particular key populations, there remains an urgent need for evidence-based policies that benefit those who are disproportionately affected by the epidemic. Two of our main areas of focus this year will be highlighting the role of data in combatting the opioid epidemic and the accompanying rise in HIV and hepatitis C infections, and addressing the persistent racial disparities that drive the spread of HIV among communities of color.

In 2019, PPO will continue to shed light on the intersection of HIV, hepatitis C, and the opioid epidemic. We will expand amfAR's Opioid & Health Indicators Database, which was launched in 2017 and is now listed as an official resource on the epidemic by multiple government agencies and is often cited in the press. In addition, we plan to host a meeting bringing together Congressional representatives with community members in areas hard hit by the opioid crisis, to discuss possible solutions. We will also offer two small grants to help increase the scale and scope of innovative local strategies addressing opioids and infectious disease.

In addition, the PPO is also helping to design and oversee a groundbreaking two-year study of pilot safe injection facilities in New York State. Though 30 years of evidence from other countries show that these facilities, where clients can inject drugs under medical supervision, nearly eliminate fatal overdoses and link people who inject drugs (PWID) to needed services without increasing drug use or crime, they remain untested in the U.S. This analysis and outreach work is already helping improve evidence-based responses to this national crisis, such as ensuring quality addiction treatment is accessible to those most in need of it.

With regard to racial disparities, the PPO will continue to speak out publicly and provide evidence on the urgent need for HIV services among racial minorities, particularly young African-American and Latino men who have sex with men (MSM). For example, black MSM represent just 0.2% of the total U.S. population, but 25% of new HIV infections. Our past efforts to publicize this issue have been highlighted in the *New York Times*, *Teen Vogue*, *NPR*, *Daily Beast*, *POZ*, and on *Washington Post Live!*, and we plan to continue similar outreach in the coming year.

Global Advocacy

On the global front, amfAR will continue to focus on its work to expand the number of people with HIV who can access the care and treatment they need. To do this, we must reach out to the U.S. government and other policymakers with influence over global health programs to make these programs as transparent and equitable as possible.

The U.S. President's Emergency Plan for AIDS Relief (PEPFAR), which is one of the biggest providers of HIV treatment in sub-Saharan Africa and beyond, will remain a primary focus of our advocacy. The PPO will continue its work to increase PEPFAR's impact and transparency by teaching community advocates in Uganda, Malawi, Kenya, Zambia, and Zimbabwe how to

interpret PEPFAR-related data—including that contained in amfAR's PEPFAR Country/Regional Operational Plan Database—to improve their advocacy efforts. The PPO team will also build a database to increase access to program information from the Global Fund to Fight AIDS, Tuberculosis and Malaria to complement our PEPFAR database.

The PPO is also working to document the effects of the U.S. government's reinstatement of the Mexico City Policy, which withholds funding from any international organizations that offer women advice on abortion. Many of these organizations also provide lifesaving HIV services that are now being jeopardized. In addition to continuing our work to understand and report the impact of the policy, PPO will work to provide links to high-quality care for individuals who have lost access to sexual and reproductive health services due to the policy.

Finally, the PPO plans to build upon the success of its 2018 analysis that used social media platforms to show that MSM are undercounted in many countries—resulting in too few HIV resources and services targeting this high-risk population. This year, the PPO will engage large tech companies (i.e., Google, Twitter, and Facebook) and other actors to discuss the positive outcomes associated with sharing data on key populations in an effort to further improve these estimates. The PPO also hopes to move the discussion forward on how population estimates can be similarly improved for transgender individuals, PWID, and female sex workers.

THE WAY FORWARD

The innovative studies described above are only a small portion of the comprehensive research effort we plan to mount in the coming year, which we believe will draw us closer to breaking down the barriers between us and a cure. In the meantime, we continue our tireless advocacy to ensure that the advances we have already made in the fight against HIV reach those who need them the most.

All the work described in this Action Plan is a reflection of our commitment to one of the most important causes of our lifetime. amfAR was founded in response to the tremendous pain, loss, anger—and courage—that characterized the early years of the AIDS crisis. We are sustained more than three decades later by the knowledge that we have transformed our losses into action, honoring our pledge to those we've lost as we work **TO MAKE AIDS HISTORY**.

The time to end AIDS is now. The way to end it is science. The power to end it is yours. Thank you for your support.

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