Scaling Up Antiretroviral Treatment Sustainably

Gilead Sciences Programs in Developing Countries

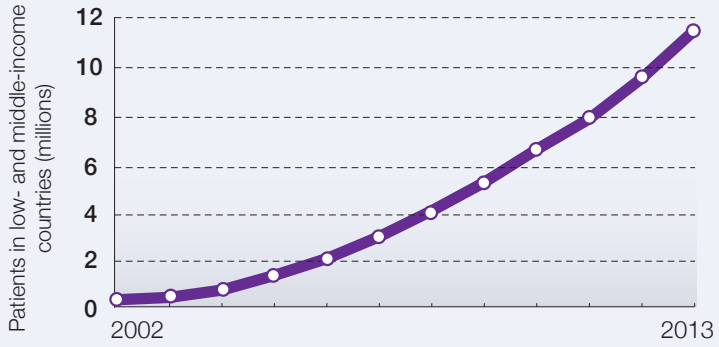
For more than a decade, Gilead Sciences has been a leader in the development of antiretroviral therapy for HIV/AIDS. Gilead researchers have developed seven commercially available HIV medications and are advancing a robust pipeline of next-generation therapeutic options.

Recognizing that the greatest need for HIV treatment is in the least-developed parts of the world, the company has put in place innovative programs and partnerships to expand global access to its medicines. Today, 6.7 million people are receiving Gilead HIV therapies in low- and middle-income countries.

HIV Treatment Needs

Thirty years since the first cases were reported, HIV/AIDS remains one of the world's foremost health challenges. Approximately 30 million people have died of AIDS, and more than 35 million people are now living with HIV.[1] The epidemic disproportionately affects the developing world, where 90 percent of people with HIV reside and the vast majority of new infections occur.[2] HIV is a barrier to social development and economic growth as it reduces life expectancy, destabilizes families and deepens poverty.[3]

Global HIV Treatment Scale-Up



Source: UNAIDS

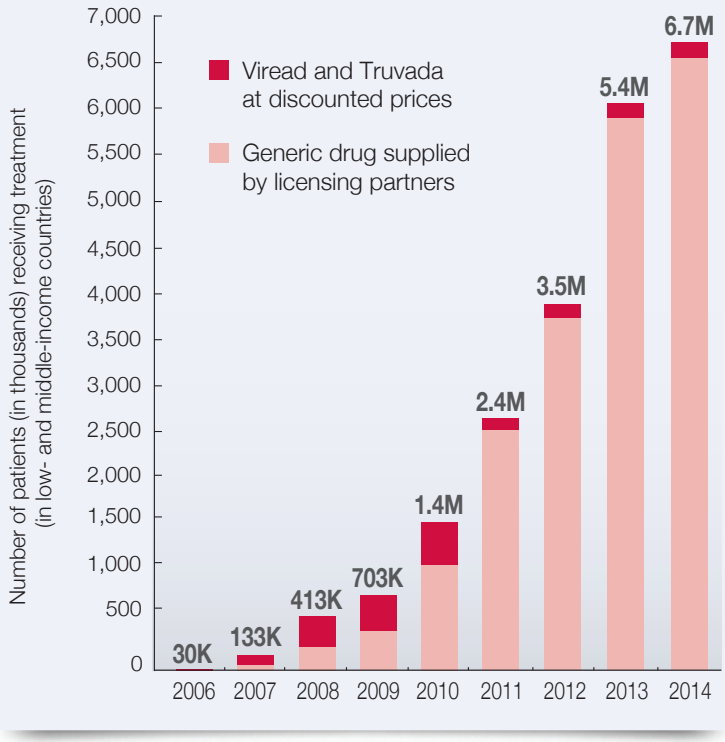
In the absence of a vaccine and cure, testing people for HIV and providing treatment to those who are infected is a primary strategy for controlling the epidemic. Over the past decade, the international community has made enormous progress in antiretroviral treatment provision: Between 2002 and 2013, the number of people in low- and middle-income countries receiving antiretroviral therapy increased from 300,000 to 11.7 million.[4,5] Treatment has averted an estimated 7.6 million AIDS deaths since 1995, and growing evidence shows that when people with HIV take effective medications to suppress the virus in their bodies, they are significantly less likely to transmit HIV to other people.[6,7]

Yet substantial needs remain, and continuing to scale up treatment is a top health and humanitarian priority. Of the 35 million people with HIV worldwide, nearly 29 million should be receiving antiretroviral therapy based on new WHO guidelines recommending earlier treatment initiation.[5]

Our Role

The Gilead corporate mission is to transform care for HIV and other life-threatening diseases. To achieve this, Gilead believes it is important to apply innovation not just to drug discovery but also to finding new ways to get affordable medicines to people in need as quickly as possible.

Access to Gilead HIV Medicines



The Gilead model for HIV treatment provision in developing countries has evolved over time, in response to lessons learned, stakeholder feedback and evidence of program effectiveness. The company's first antiretroviral access programs were based closely on the company's commercial operations in developed markets, but did not take account of the unique challenges facing drug delivery in resource-limited settings. Significant adjustments to the model have been made since then, driving year-on-year growth in the number of patients receiving Gilead HIV medicines in low- and middle-income countries.

Gilead learned early on the importance of partnership and collaboration for increasing drug access. Today, Gilead works with more than 70 manufacturers, regional and local distributors and generic licensees to expand access to marketed medicines and plan for future access to pipeline products. Within Gilead, a dedicated international business unit supports partners.

Tiered Pricing and Regional Business Partners

From the outset, a key principle of our HIV treatment access efforts has been tiered pricing of branded medicines based on a country's ability to pay. Developing countries are divided into two pricing tiers – low-income and lower middle-income – based on national income and HIV prevalence. Prices in the low-income tier account only for production cost and do not return a profit.

Viread® (tenofovir disoproxil fumarate, or TDF) has been available at reduced prices in developing countries since 2003, and Truvada® (emtricitabine co-formulated with TDF) was added in 2004, following its approval in the United States. Today, discounted Viread and Truvada are available in 125 countries that together account for 95 percent of people living with HIV in the developing world. Viread and Truvada are among the most widely used HIV medicines globally and are recommended as preferred components of antiretroviral therapy regimens in HIV treatment guidelines.[8]

To securely and efficiently distribute HIV medicines worldwide, Gilead began working in 2005 with a network of regional business partners. These include manufacturing partners in the Bahamas and South Africa licensed by the U.S. Food and Drug Administration (FDA) and regional and local distribution partners covering Africa, Asia, the Caribbean, Eastern Europe, Latin America, the Middle East and the Pacific region.

Branded Pricing Tiers

Product	Tier	Price (monthly)
Viread	Low-Income	$17.00
	Lower Middle-Income	$30.00
Truvada	Low-Income	$26.25
	Lower Middle-Income	$45.00

Gilead transfer price (USD)

Key Partners

Regional Distributors

- Amba Pharmaceuticals
- Anspec
- Aspen Pharmacare
- B&O Pharma
- Delta Medical
- Gador
- Global Pharmaceutical Exchange
- Key Oncologics
- LF Asia
- Medical Access
- MedImport
- Mylan Pharmaceuticals
- OPV Pharmaceutical
- Phillips Pharmaceuticals
- Puerto Rico Pharmaceutical
- Pulse Pharmaceuticals
- Quadri Pharma
- Rite Chem
- Stendhal
- Sterelin Medical and Diagnostics

Generic Licensees

- Alkem Laboratories
- Aspen Pharmacare
- Aurobindo Pharma*
- Cadila Healthcare
- Cipla Ltd*
- Desano Pharmaceuticals
- Emcure Pharmaceuticals*
- Hetero Labs*
- Laurus Labs*
- Mcneil & Argus Pharmaceuticals
- Micro Labs
- Mylan Laboratories
- Ranbaxy Laboratories
- SeQuent Scientific
- Shanghai Desano*
- Shasun Pharmaceuticals*
- Shilpa Medicare*
- Strides Arcolab
- Unimark Remedies

*Licensed via Medicines Patent Pool

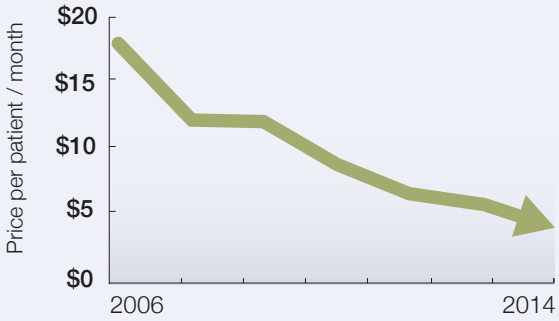
Regional business partners are the on-the-ground interface between Gilead and local governments, medical organizations and other stakeholders. In addition to delivering treatment, partners help register medicines with regulatory authorities, ensuring that dossiers conform to national requirements and are processed efficiently, and assist with medical and clinical education. Gilead provides technical, medical and marketing support to strengthen partners' capabilities in these areas, and distributors are permitted to add a marginal markup to the prices of Gilead products they sell.

Importance of Voluntary Generic Licensing

Gilead recognizes that on its own, the company does not have sufficient capacity to meet global needs for HIV treatment in a cost-effective manner. For this reason, in 2006 Gilead began entering into voluntary licensing agreements with Indian manufacturers, granting them rights to produce and sell high-quality, low-cost generic versions of Gilead medicines. The vast majority of Gilead HIV therapies used in developing countries – 99 percent – are now generic products produced by licensees.

Under the terms of licensing agreements (available at www.gilead.com), partners are able to produce generic TDF-based HIV therapy for sale in 112 low- and middle-income countries. Partners set their own prices and may also create fixed-dose combinations with other HIV medicines. Partners receive a full technology transfer of the Gilead manufacturing process, enabling them to quickly scale up production.

Lowest TDF Price



Generic licensee selling prices (USD)

To support the licensing program, Gilead receives a three-percent royalty on sales of finished goods, which is reinvested in product registration, medical education and other activities undertaken on behalf of licensees. The royalty is waived, however, on pediatric formulations as an incentive to help partners develop generic versions of HIV treatment appropriate for children.

In July 2011, Gilead became the first innovator pharmaceutical company to sign an agreement with the Medicines Patent Pool (MPP), an international organization that expands access to medicines through the sharing of drug patents (see www.medicinespatentpool.org for details). Under the current agreements, generic drug manufacturers in India and China may develop and distribute Gilead's marketed HIV and hepatitis B medicines in 112 developing countries. In its 2011 annual report, MPP said Gilead has set "new public health standards, beyond any previous voluntary licensing agreement with a pharmaceutical company" for transparency, scope, pipeline products and flexibility.[9]

Medicines Licensed in 2011

Vitekta®	elvitegravir
Tybost®	cobicistat
Stribild® single tablet regimen	elvitegravir / cobicistat / TDF / emtricitabine

Currently, 17 Indian manufacturers, one South African and one Chinese company hold licenses to Gilead HIV medicines. Licensees have received more than 30 World Health Organization pre-qualifications and/or FDA tentative approvals for their products. Extension of non-exclusive licenses to multiple manufacturers has promoted competition to produce large volumes of high-quality medicines at low prices. Over the past eight years, licensing partners have lowered prices by 80 percent, and the lowest price of generic Viread is currently US $4.00 per patient per month. These price reductions have translated into cost savings for HIV treatment programs.

As next-generation drugs advance through the research and development pipeline, Gilead evaluates opportunities to include them in access programs, including voluntary generic licensing. In July 2014, Gilead expanded its MPP licensing agreements by granting generic manufacturers in India and China future rights to develop its investigational drug, tenofovir alafenamide (TAF), for the treatment of HIV and hepatitis B in 112 resource-limited countries, contingent on the medicine's U.S. regulatory approval. In September 2014, MPP announced that it signed sub-licensing agreements with five Indian and one Chinese company to develop TAF for distribution in developing countries upon its regulatory approval.

Working Locally to Advance Access

Lowering prices is just one part of successfully scaling up HIV treatment. Also critical are in-country activities that support drug availability and use, including product registration, medical and clinical education, demand forecasting and collaborative research. All of these are elements of our treatment access initiatives.

- **Product Registration:** Gilead invests considerable resources to register its HIV products with regulatory authorities in each developing country included in access programs. Regional business partners help manage national registration processes, which can vary widely across countries, and assist with pharmacovigilance and safety reporting once registrations are obtained. Viread and Truvada are now registered in 109 developing countries. (Monthly updates are posted at www.gilead.com.)
- **Medical and Clinical Education:** In 2010-2011, Gilead and regional business partners conducted more than 80 medical and clinical education events in developing countries to increase knowledge of Gilead HIV therapies. Gilead also provides a number of printed and online medical education resources.
- **Demand Forecasting:** Ensuring an uninterrupted supply of antiretroviral therapy requires accurately forecasting product demand. Gilead has invested in proprietary information tools to track orders and inventory across regions and avoid supply stockouts. Gilead also has strong relationships with organizations such as the Clinton Health Access Initiative that help coordinate large-scale purchasing of HIV treatment.

Medical Education Resources

Information for healthcare providers translated into local languages*

Patient education aids adapted for low-literacy populations*

HiV-Link – medical information questions answered via text message

*Images of access materials for Africa

- **Collaborative Research:** Gilead supports clinical research studies to examine the optimal use of HIV treatment in developing countries. These have included studies investigating how to reach more patients with therapy by streamlining clinical procedures, and studies examining the potential benefits of starting patients on therapy earlier that is now standard practice. Gilead also donated Viread and Truvada for clinical trials evaluating the effectiveness of antiretroviral agents for reducing the risk of acquiring HIV when taken by high-risk uninfected individuals, a strategy known as pre-exposure prophylaxis (PrEP). (With the exception of Truvada in the United States, PrEP is an investigational strategy.)

Looking Ahead

Our company's work in developing countries has contributed significantly to the global scale-up of antiretroviral treatment, and continues to evolve in response to new challenges and opportunities.

Sharing information and seeking outside input are vital to the success of drug access efforts, and Gilead will continue consulting with diverse stakeholders on ways to strengthen access programs and partnerships. As next-generation therapies receive regulatory approval, Gilead will work diligently to minimize the time it takes for them to reach patients in the developing world.

Many barriers remain to further expanding HIV treatment, although momentum is on the side of progress. There is now clear evidence that treatment scale-up can help turn the tide of the epidemic, and that treating more people can help reduce AIDS deaths and prevent new HIV infections.[10,11] Achieving the goal of universal access to HIV treatment is within reach, and has never been more important.

References

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[6] UNAIDS. The Gap Report (2014)

[7] Cohen, M., et al. Prevention of HIV-1 infection with early antiretroviral therapy. New England Journal of Medicine, 2011;365:493-505.

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[10] Schwartlander, B., et al. Towards an improved investment approach for an effective response to HIV/AIDS. Lancet (2011).

[11] Nosyk, B., and Montaner, J. The evolving landscape of the economics of HIV treatment and prevention. PLoS Medicine (2012).

Gilead Access Countries

Afghanistan
Angola
Anguilla
Antigua & Barbuda
Aruba
Bahamas
Bangladesh
Barbados
Belize
Benin
Bhutan
Bolivia
Botswana
British Virgin Islands
Burkina Faso
Burundi
Cambodia
Cameroon
Cape Verde
Cayman Islands
Central African Republic
Chad
Comoros
Congo, Dem. Republic of
Congo, Republic of
Cuba
Curacao
Djibouti
Dominica
Dominican Republic
Ecuador
El Salvador
Equatorial Guinea
Eritrea
Ethiopia
Gabon
Gambia
Ghana
Grenada
Guatemala
Guinea
Guinea Bissau
Guyana
Haiti
Honduras
India
Indonesia
Ivory Coast
Jamaica
Kenya
Kiribati
Kyrgyzstan
Laos
Lesotho
Liberia
Madagascar
Malawi
Maldives
Mali
Mauritania
Mauritius
Mongolia
Montserrat
Mozambique
Myanmar
Namibia
Nauru
Nepal
Nicaragua
Niger
Nigeria
North Korea
Pakistan
Palau
Panama
Papua New Guinea
Paraguay
Peru
Philippines
Rwanda
Saint Kitts and Nevis
Saint Lucia
Samoa
Sao Tome & Principe
Senegal
Seychelles
Sierra Leone
Solomon Islands
Somalia
South Africa
South Sudan
Sri Lanka
St. Maarten
St. Vincent & Grenadines
Sudan
Suriname
Swaziland
Tajikistan
Tanzania
Thailand
Timor-Leste
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Trinidad and Tobago
Turkmenistan
Turks and Caicos
Tuvalu
Uganda
Uzbekistan
Vanuatu
Vietnam
Zambia
Zimbabwe

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Mexico
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Tunisia
Uruguay
Venezuela