

# 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 11 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, 10 million people are receiving Gilead HIV therapies in low- and middle-income countries.

## HIV Treatment Needs

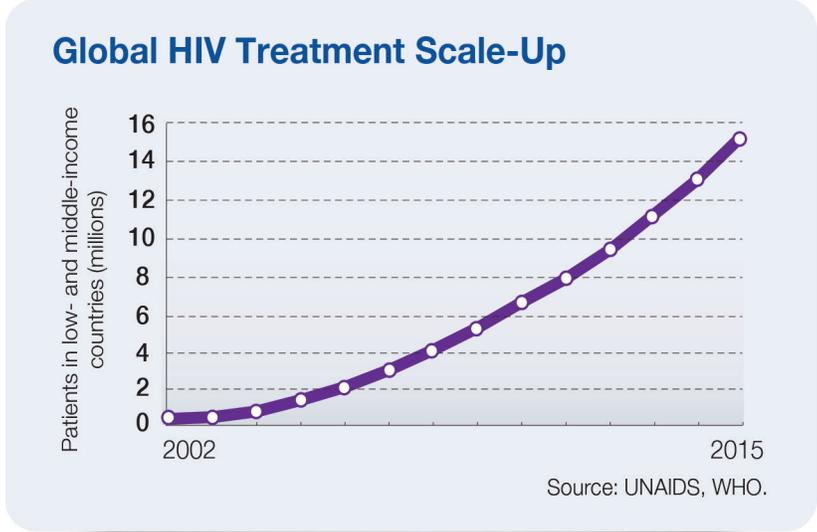
More than thirty years since the first cases were reported, HIV/AIDS remains one of the world's foremost health challenges. More than 35 million people have died of AIDS, and nearly 37 million people are now living with HIV.<sup>1</sup> The epidemic disproportionately affects the developing world, where 90 percent of people with HIV reside and the vast majority of new infections occur.<sup>2</sup> HIV is a barrier to social development and economic growth as it reduces life expectancy, destabilizes families and deepens poverty.<sup>3</sup>

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. For more than a decade, the international community has made enormous progress in antiretroviral treatment provision: Between 2002 and 2015, the number of people in low- and middle-income countries receiving antiretroviral therapy increased from 300,000 to 15.3 million.<sup>4,5</sup> Treatment has averted an estimated 7.8 million AIDS deaths since 2000, 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.<sup>6,7</sup>

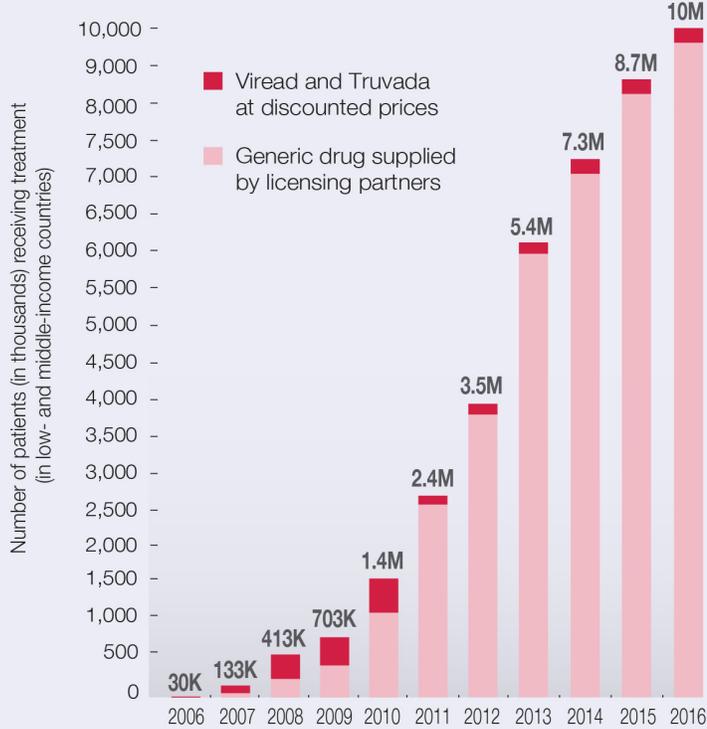
Yet substantial needs remain, and continuing to scale up treatment is a top health and humanitarian priority. The World Health Organization recently released new guidelines recommending immediate treatment for all, meaning that 20 million people worldwide are still in need of antiretroviral therapy.<sup>8,9</sup>

## 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 and HIV epidemiology. Developing countries that are classified as low-income or lower-middle-income by World Bank, as well as those with significant unmet HIV/AIDS disease burden, are designated as access countries (see list at the back of document). Prices in the access countries account only for production and other related costs 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 134 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.<sup>10</sup>

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.

### Access Pricing

Product	Price (monthly)
<b>Viread</b>	\$15.00
<b>Truvada</b>	\$20.00



Gilead transfer price (USD)

## Key Partners

### Regional Distributors

- Amba Pharmaceuticals
- Aspen Pharmacare
- Dinafa
- Execu Regulatory Services
- Ferozsons Laboratories
- Gador S.A.
- Global Pharmaceutical Exchange
- Ibis Pharma
- Key Oncologics
- Laboratoire B&O
- LF Asia
- Medical Access Uganda
- MedImport
- MSJ Ltd. (Unicorn)
- Mylan Pharmaceuticals
- Oduber
- OPV Pharmaceutical
- Phillips Pharmaceuticals
- Puerto Rico Pharmaceuticals
- Pulse Pharmaceuticals
- Quadri Pharma
- Rite Chem
- Stendhal
- Sterelin Medical & Diagnostics
- Soho
- Tridem
- United Medical
- Xixia

### Generic Licensees

- Alkem Laboratories Ltd
- Aspen
- Aurobindo Pharma Limited\*
- Cadila Healthcare Ltd
- Cipla Ltd\*
- Emcure Pharmaceuticals Limited\*
- Hetero Labs Ltd\*
- Laurus Labs Ltd\*
- Lupin Limited\*
- Mcneil & Argus Pharmaceuticals
- Micro Labs\*
- Mylan Laboratories Limited
- SeQuent Scientific Limited
- Shanghai Desano\*
- Strides Shasun Ltd
- Sun
- Unimark Remedies Ltd
- Zhejiang Huahai Pharmaceutical Co Ltd\*

\*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

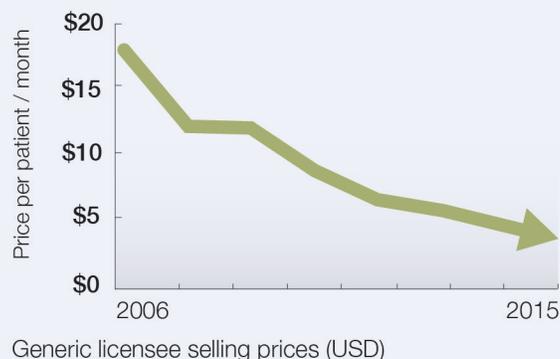
Gilead recognizes that on its own, the company does not have sufficient capacity to meet global needs for HIV treatment in a cost-effective manner. For this reason, in 2006 Gilead began entering into voluntary licensing agreements with Indian manufacturers, granting them rights to produce and sell high-quality, low-cost generic versions of Gilead medicines. The vast majority of Gilead HIV therapies used in developing countries – 98 percent – are now generic products produced by licensees.

Under the terms of the licensing agreements (available at [www.gilead.com](http://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.

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](http://www.medicinespatentpool.org) for details). Under the current agreements, generic drug manufacturers in India, China and South Africa 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.<sup>11</sup>

### Lowest TDF Price



## Gilead Licensed Medicines

<b>Viread®</b>	TDF
<b>Vitekta®</b>	elvitegravir
<b>Tybost®</b>	cobicistat
<b>Stribild® single tablet regimen</b>	elvitegravir / cobicistat / TDF / emtricitabine
<b>Genvoya® single tablet regimen</b>	elvitegravir / cobicistat / TAF / emtricitabine
<b>Descovy®</b>	emtricitabine / tenofovir alafenamide

Currently, 15 Indian manufacturers, one South African and two Chinese companies 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 10 years, licensing partners have lowered prices by 80 percent, and the lowest price of generic Viread is currently US \$3.50 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. To that end, Gilead has signed licenses with generic companies and the MPP granting manufacturers future rights to produce and market generic versions of Gilead products upon FDA approval. For example, Gilead expanded its MPP licensing agreements in July 2014 by granting generic manufacturers in India, China and South Africa rights to develop its investigational compound, tenofovir alafenamide (TAF) for the treatment of HIV and hepatitis B in 112 countries. Licensed manufacturers can now produce TAF as part of any treatment combination they see fit, following the November 2015 FDA approval of the TAF-containing single tablet regimen Genvoya.

## 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. Gilead now has 264 HIV medicine registrations in developing countries. (Monthly updates are posted at [www.gilead.com](http://www.gilead.com).)
- **Medical and Clinical Education:** Gilead and regional business partners conduct 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 than was 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).

## 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.<sup>12,13</sup> Achieving the goal of universal access to HIV treatment is within reach, and has never been more important.

### References

- <sup>1</sup> World Health Organization (WHO). HIV/AIDS Fact sheet N°360. July 2016. Available at: <http://www.who.int/mediacentre/factsheets/fs360/en/>.
- <sup>2</sup> UNAIDS. UNAIDS Report on the Global AIDS Epidemic (2010).
- <sup>3</sup> UNAIDS. Report on the Global AIDS Epidemic (2008).
- <sup>4</sup> WHO. A Commitment to Action for Expanded Access to HIV/AIDS Treatment (2002).
- <sup>5</sup> UNAIDS. Get on the Fast-Track: the life-cycle approach to HIV (2016).
- <sup>6</sup> UNAIDS. How AIDS Changed Everything (2015).
- <sup>7</sup> Cohen, M., et al. Prevention of HIV-1 infection with early antiretroviral therapy. *New England Journal of Medicine*, 2011;365:493-505.
- <sup>8</sup> WHO. Guideline On When To Start Antiretroviral Therapy And On Pre-Exposure Prophylaxis For HIV (2015).
- <sup>9</sup> UNAIDS. AIDS by the numbers 2016 (2016).
- <sup>10</sup> WHO. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection (2016).
- <sup>11</sup> Medicines Patent Pool. Stimulating Innovation, Expanding Access, Improving Health: Annual Report 2010-2011 (2012).
- <sup>12</sup> Schwartlander, B., et al. Towards an improved investment approach for an effective response to HIV/AIDS. *Lancet* (2011).
- <sup>13</sup> Nosyk, B., and Montaner, J. The evolving landscape of the economics of HIV treatment and prevention. *PLoS Medicine* (2012).

## Gilead Access Countries

Afghanistan	Guinea
Algeria	Guinea Bissau
Angola	Guyana
Anguilla	Haiti
Antigua & Barbuda	Honduras
Armenia	India
Aruba	Indonesia
Bahamas	Ivory Coast
Bangladesh	Jamaica
Barbados	Kenya
Belize	Kiribati
Benin	Kyrgyzstan
Bhutan	Laos
Bolivia	Lesotho
Botswana	Liberia
British Virgin Islands	Libya
Burkina Faso	Madagascar
Burundi	Malawi
Cambodia	Maldives
Cameroon	Mali
Cape Verde	Marshall Islands
Cayman Islands	Mauritania
Central African Republic	Mauritius
Chad	Micronesia
Comoros	Moldova
Congo, Dem. Republic of	Mongolia
Congo, Republic of	Montserrat
Cook Islands	Morocco
Cuba	Mozambique
Curacao	Myanmar
Djibouti	Namibia
Dominica	Nauru
Dominican Republic	Nepal
Ecuador	Nicaragua
Egypt	Niger
El Salvador	Nigeria
Equatorial Guinea	North Korea
Eritrea	Pakistan
Ethiopia	Palau
Fiji	Papua New Guinea
Gabon	Paraguay
Gambia	Philippines
Georgia	Rwanda
Ghana	Saint Kitts and Nevis
Grenada	Saint Lucia
Guatemala	Samoa

## Emerging Markets

Sao Tome & Principe	Argentina
Senegal	Brazil
Seychelles	Chile
Sierra Leone	Colombia
Solomon Islands	Costa Rica
Somalia	Mexico
South Africa	Panama
South Sudan	Peru
Sri Lanka	Uruguay
St. Maarten	Venezuela
St. Vincent & Grenadines	
Sudan	
Suriname	
Swaziland	
Tajikistan	
Tanzania	
Thailand	
Timor-Leste	
Togo	
Tonga	
Trinidad and Tobago	
Tunisia	
Turkmenistan	
Turks and Caicos	
Tuvalu	
Uganda	
Ukraine	
Uzbekistan	
Vanuatu	
Vietnam	
Zambia	
Zimbabwe	