Responses of Mr. Daniel O'Day, Chairman and Chief Executive Officer of Gilead Sciences, Inc., to Questions for the Record in the May 16, 2019, Hearing of the U.S. House of Representatives Committee on Oversight and Reform

July 15, 2019

Chairman Elijah E. Cummings

1. *Please provide a breakdown of Truvada for pre-exposure prophylaxis (PrEP)-user data by payment source—including private insurance, Medicaid, Medicare, Veterans Affairs, TRICARE, and Gilead's patient and copay assistance programs.*

Due to medical privacy protections and other limitations, Gilead is not always able to determine whether Truvada is being prescribed for treatment or for PrEP.[1] Relying on external data available to the company and other sources, Gilead estimates that sales of Truvada for PrEP in 2018 were distributed among payer segments as follows:

Commercial/ Exchange	Medicare Part D	Managed Medicaid	FFS Medicaid	FSS	340B/PHS, Other
65%	4%	6%	4%	3%	18%

2. *Please provide any data Gilead has collected on insurance denials of Truvada or Truvada for PrEP.*

Drawing on third-party national claims data, in the last year, Gilead estimates that fewer than 4% of such claims in the four major payment segments (*i.e.*, commercial, Medicare, Medicaid, and managed Medicaid) were denied due to an insurer's formulary or plan design.

With respect to Truvada generally (whether treatment or PrEP), in each of the last four calendar quarters (*i.e.*, Q2 2018 through Q1 2019), insurers rejected about 3% of claims submitted by patients seeking the drug for the first time for formulary-related reasons. Formulary-related rejections are denials of coverage resulting from limitations on insurance coverage or plan design, including instances in which a drug is not included on an insurer's formulary or not covered by a patient's plan, as well as claims denied due to a patient's failure to seek prior authorization or an insurer's denial of a request for prior authorization. Overall rejection rates, including both formulary-related rejections and other denials of coverage not tied to the drug itself (*e.g.*, rejections due to the submission of incorrect paperwork or other similar issues) ranged between 9.9% and 10.7% during this period.

Rejection rates for Truvada for PrEP are generally consistent with rates for Truvada prescribed to treat HIV. During the last four calendar quarters, the rate of formulary-related rejections for Truvada for PrEP ranged between 3.3% and 3.5%, while the overall rejection rate varied between 10.3% and 11.5%.

[1] Truvada, Truvada for PrEP, Viread, and Emtriva are registered trademarks of Gilead.

Representative Katie Hill

1. *Please describe trends over the past ten years in uptake of Gilead's patient and copay assistance programs, excluding expected gains for the additional 200,000 individuals who will be supported by Gilead's recent* Ending the Epidemic *donation.*

Through its Advancing Access Program, Gilead provides access to call center associates who can help individuals understand their insurance coverage, answer insurance-related questions, provide information about the Affordable Care Act and exchange plan enrollment process, and more. Beyond these general offerings, the Advancing Access Program offers individuals with private, commercial insurance copay assistance to obtain Truvada or Truvada for PrEP. Further, eligible uninsured or underinsured individuals who earn less than five times the federal poverty level may also receive free Truvada for treatment or for PrEP through the Advancing Access Program.

For the years 2009 through 2018, the following chart indicates (1) the number of individuals per year who utilized Gilead's copay assistance program to obtain Truvada (for treatment or PrEP); (2) the number of individuals per year to whom Gilead provided free Truvada for treatment through its Patient Assistance Program ("PAP"); (3) the number of individuals per year to whom Gilead provided free Truvada for PrEP through PAP; and (4) the total number of individuals per year to whom Gilead provided some form of direct assistance to help individuals access their prescribed Truvada.[2]

[2] These figures represent the number of new enrollments in each of Gilead's Truvada-focused patient support programs in a given year. In some cases, an individual may enroll in more than one such program or may enroll in the same program multiple times in the same calendar year. In such cases, each of these distinct enrollments would be reflected in the chart above.

Number of Individuals Receiving Financial Assistance Through Gilead's Truvada-Related Patient Support Programs

Year	Copay Assistance[3]	Free Truvada Through PAP	Free Truvada for PrEP Through PAP[4]	Total Truvada Assistance
2019[5]	160,997	611	15,518	177,126
2018	170,577	997	26,796	198,370
2017	132,777	1,144	15,758	149,679
2016	101,674	1,617	7,527	110,818
2015	63,077	1,868	2,758	67,703
2014	36,381	2,378	723	39,482
2013	25,133	2,880	176	28,189
2012	19,844	4,777	17	24,638
2011	788	5,762	N/A	8,631
2010	N/A	4,190	N/A	4,505
2009	N/A	949	N/A	1,155

Through Gilead's patient assistance programs, the company has provided free Truvada for treatment or for PrEP to more than 66,500 unique patients since 2009. This total does not include individuals receiving free Truvada for PrEP through Gilead's recently announced donation in support of the Administration's *Ending the Epidemic* initiative.

2. *In your written testimony, you stated that Gilead invested approximately "$1.1 billion on R&D related to Truvada" since 2000. What percentage of this $1.1 billion investment was dedicated to research on Truvada's designation for pre-exposure prophylaxis (PrEP)?*

Gilead estimates that it spent approximately $25 billion on research and development since 2000, of which the company estimates that $1.1 billion was devoted to research and development related to Truvada. This estimate reflects total research and development expenditures associated with Truvada based on available accounting information maintained by the company.

Gilead's earliest HIV-focused research focused on the development of effective therapies to treat the disease and prolong the lives of people who were already infected. This research ultimately led to the development of tenofovir disoproxil fumarate ("TDF"), which Gilead combined with emtricitabine ("FTC") to create Truvada. The launch of Truvada thus represented the culmination of more than a decade of work undertaken by Gilead scientists between the early 1990s and mid-2000s. Whether it is administered after infection, shortly after someone has been exposed to HIV (*i.e.*, post-exposure prophylaxis, or "PEP"), or before someone anticipates being exposed to HIV (*i.e.*, PrEP), Truvada works in exactly the same way in the human body. For that reason, the research and development that led to the invention of

[3] Gilead initiated its copay assistance program for its HIV treatment therapies in August 2011.

[4] The FDA approved the use of Truvada for PrEP in July 2012.

[5] Copay assistance figures are current through June 30. PAP figures are current through June 26.

Truvada as a treatment medication was essential to, and largely coextensive with, related research demonstrating the drug's efficacy as a tool to prevent HIV infection.

Gilead recognized as early as the mid-1990s that tenofovir held potential promise as a means of blocking the transmission of HIV to those not yet exposed to the virus. With this in mind, Gilead led an effort to assist two NIH-funded studies conducted at the University of Washington designed to assess the efficacy of tenofovir for prophylactic use. For example, Gilead donated all of the drug used in these studies, collaborated in the study methodology design, provided dosing guidance, and participated in analysis of the study results. These studies demonstrated that tenofovir was effective as both a pre- and post-exposure prophylactic, with Gilead's head of research and development at the time credited as an author when one of the studies was published in *Science*.[6]

In the years that followed, Gilead continued to develop innovative HIV treatment therapies while supporting PrEP-focused research led by public health authorities and others. In particular, among other clinical trials devoted to the use of Truvada for PrEP, Gilead provided free drugs and technical assistance to the Preexposure Prophylaxis Initiative (iPrEx) clinical trial funded by the National Institutes of Health and the Bill and Melinda Gates Foundation. As before, in recognition of their substantial contributions to the study, two Gilead researchers were listed as co-authors of the study upon its publication.[7]

In addition, Gilead continues to provide financial support to third-party investigators researching a variety of scientific, sociocultural, and implementation questions related to Truvada for PrEP or HIV prevention generally. This support has helped to advance understanding of PrEP use and the implementation of PrEP programs, as well as studies focused on at-risk populations with unmet need such as people of color, trans people, adolescents, and sex workers. Gilead also regularly provides Truvada at no cost to third parties for use in clinical trials related to Truvada for PrEP. Between 2012 and the first quarter of 2019, Gilead provided more than 100,000 bottles (one-month supply) for use in clinical research related to Truvada for PrEP, including two large, NIH-funded, HIV Prevention Trials Network studies designed to support regulatory approval of non-Gilead products.

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[6] Che-Chung Tsai et al., *Prevention of SIV Infection in Macaques by (R)-9-(2-Phosphonylmethoxypropyl)adenine*, 270 Science, Nov. 17, 1995, at 1197, *available at* https://science.sciencemag.org/content/270/5239/1197.

[7] Robert M. Grant et al., *Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men*, 363 N. Engl. J. Med. 2587 (2010), *available at* https://www.nejm.org/doi/full/10.1056/NEJMoa1011205.

Representative Alexandria Ocasio-Cortez

1. *Mr. O'Day, at the hearing you testified that Gilead spent $1.1 billion on the research and development of Truvada. Your employer, Gilead Sciences, Inc., has publicly stated the same number in a company press release.*

    a. *Does this figure include any promotional, advertising, or educational costs involving Viread, Emtriva, and/or Truvada? If it does, what proportion of the $1.1 billion figure was spent on such costs?*

Gilead's estimate of the total research and development costs associated with Truvada does not include marketing, educational, or other promotional expenses.

    b. *Does this figure include licensing costs, or other costs related to the use of tenofovir? If it does, what proportion of the $1.1 billion figure was spent on such costs?*

Gilead's estimated research and development expenses associated with Truvada do not include licensing or other acquisition costs, including the company's $525 million acquisition of Triangle Pharmaceuticals, through which Gilead obtained the right to develop and commercialize emtricitabine, one of the two components of Truvada. Likewise, Gilead's estimated research and development investments related to Truvada do not include the millions of dollars in royalties paid to the Institute of Organic Chemistry and Biochemistry and the Rega Institute for Medical Research in connection with a longstanding licensing agreement between these entities and Gilead. Gilead licensed the rights to a portfolio of nucleotide compounds, including tenofovir, from these entities in 1991.

    c. *What proportion of the $1.1 billion figure was spent on clinical trials related to the Food and Drug Administration (FDA) approval of Viread? Please specify the expenditures for each specific trial, including the GS-98-902 trial, the GS-98-907 trial, the GS-99-908 trial, Study 701, and Study 901.*

In total, Gilead incurred approximately $389 million in external expenses associated with these studies. Because Gilead does not maintain trial-specific accounting data for research and development conducted prior to 2009, the company is unable to determine what portion of this total was devoted to each of the listed trials.

    d. *What proportion of the $1.1 billion figure was spent on clinical trials related to the FDA approval of Emtriva? Please specify the expenditures for each specific trial, including the FTC-301A and FTC-303 trials.*

In total, Gilead incurred approximately $78 million in external expenses associated with these studies. Because Gilead does not maintain trial-specific accounting data for research and development conducted prior to 2009, the company is unable to determine what portion of this total was devoted to each of the listed trials.

    e. *What proportion of the $1.1 billion figure was spent on clinical trials related to the FDA approval of Truvada? Please specify the expenditures for each specific trial.*

In total, Gilead incurred approximately $229 million in external expenses associated with these studies. Because Gilead does not maintain trial-specific accounting data for research

and development conducted prior to 2009, the company is unable to determine what portion of this total was devoted to each of the listed trials.

f. What proportion of the $1.1 billion figure was spent on clinical trials related to the FDA approval of Truvada as PrEP? Please specify the expenditures for each specific trial.

See the response to Representative Hill's question #2, above.

2. You testified repeatedly about TAF, an active ingredient in Genvoya, Odefsey, Descovy, Vemlidy, and Biktarvy, which you characterized as a "new" drug. Although the first TAF containing drug, Genvoya, would not be FDA-approved until 2015, Gilead discovered TAF before 2001, when Gilead researchers published data regarding the metabolism of TAF in a peer reviewed journal. In light of this discrepancy, please answer the following questions:

a. Gilead announced the discontinuation of the development of TAF on October 21, 2004, claiming that "Gilead does not believe that [TAF] has a profile that differentiates it [from TDF] to an extent that supports its continued development." Yet on March 2, 2011, your predecessor, Dr. John Milligan, claimed that the company discontinued development of TAF because it did not want to suggest that "Viread [TDF] wasn't the safest thing on the market." Why did Gilead stop the development of TAF in 2004, only to resume it later?

Prior to the launch of Truvada, Gilead was focused on developing medications for the treatment of HIV. At the time, patients were dying daily from AIDS and HIV/AIDS-related complications, and Gilead was committed to working aggressively to bring improved treatments to market to prolong the lives of people living with the disease.

After licensing the rights to tenofovir in 1991, Gilead spent nearly a decade developing the compound into a drug that could be used to treat HIV. During this process, Gilead screened more than 100 tenofovir-based compounds for toxicity and appropriate antiviral activity before ultimately selecting TDF for further development. Following promising results in Gilead-sponsored pre-clinical and clinical trials, the company moved forward with bringing TDF to market as an HIV treatment therapy. As a result of these efforts, Gilead obtained FDA approval of TDF as the first tenofovir-based therapy in October 2001 and began marketing the drug as Viread.

Late in the TDF development process, as the drug entered clinical trials, Gilead began investigating compounds to serve as alternative therapies should TDF prove unsuitable for clinical use. Through this work, Gilead discovered TAF in the late 1990s and patented the drug shortly thereafter. As the TDF clinical trials proved successful, Gilead—which was a much smaller company at the time, with a more limited research and development budget—focused its efforts on developing combination HIV therapies containing TDF and investigating other agents to combine with TDF to create a single-pill regimen. Accordingly, Gilead concentrated on developing and expanding access to life-saving treatment therapies, which was the most pressing issue at the time. These efforts ultimately resulted in the approval of Truvada as one of the first fixed-dose combination pills for use in HIV treatment in August 2004, and the approval of Atripla as the first fixed-dose single-pill regimen for HIV therapy in July 2006. In 2006, five

years after Viread was launched, experts continued to tout TDF-containing regimens as having "minimal side effects or long-term toxicity."[8]

As a result of the success of Viread and other TDF-based therapies, and as the life expectancy of patients with HIV continued to increase, Gilead saw a need for an evolution in therapy that served the evolving patient population. For example, as individuals aged, the potential for renal and bone toxicity with long-term TDF use became more apparent. As such, a new need arose to develop drugs that accounted for the extended life expectancy of persons living with HIV and the normal aging process. Because of that new need, TAF became a compound worth reevaluating. As such, consistent with its commitment to developing innovative HIV treatment therapies, Gilead devoted resources to further research TAF. Those efforts led to the development and FDA approval of the four TAF-based combination therapies currently manufactured by Gilead.

b. If Gilead had not discontinued development of TAF in 2004, when did the company estimate it would have been approved by the FDA?

As described above, after TAF was initially identified as a potential alternative to TDF, TDF's success in a clinical setting led Gilead to prioritize the development of Viread and the TDF-based combination therapies that changed the course of the HIV epidemic. Given the very early stage of development of TAF at the time, as well as the regulatory uncertainty inherent in the development and approval of any new compound, it is unclear how long it would have taken for Gilead to obtain FDA approval of TAF had the company pursued development continuously instead of focusing on expanding access to TDF-based therapies.

c. Given that TAF is nearly two decades old, why did you refer to it as a new drug?

In my testimony, I was referring to TAF-based therapeutic drug treatment, not the underlying chemical compound. Although the TAF molecule was discovered and patented nearly two decades ago, significant research, development, and investment were needed to transform that molecule into a component of combination therapies approved by the FDA to treat or prevent HIV. Doing so required Gilead to invest in additional clinical trials and seek FDA approval of TAF-based therapies, neither of which were guaranteed to succeed. These risks notwithstanding, and consistent with the company's commitment to improving treatments for people living with HIV and addressing unmet medical need, Gilead pushed ahead and successfully developed multiple new HIV treatment therapies containing TAF that were launched as new medications, the first of which was approved by the FDA in 2015.

3. During your testimony, you claimed that the patents the Centers for Disease Control and Prevention holds protecting tenofovir and emtricitabine to prevent HIV infection are invalid. Under federal law, patents are presumed valid if asserted in federal court. Why do you believe these patents are not valid? If you believe prior art would invalidate these patents, please provide specific examples of such.

Researchers at Gilead and elsewhere recognized as early as the mid-1990s that tenofovir-based compounds like Truvada held potential promise as a means of preventing transmission of HIV. Soon after the approval of Truvada for treatment—and well before the U.S. Centers for

[8] Press Release, Johns Hopkins Medicine, Study Sets New Gold Standard for Initial Antiretroviral Treatment of HIV Infection (Jan. 18, 2006), *available at* https://www.hopkinsmedicine.org/Press_releases/2006/01_18_06.html.

Disease Control and Prevention ("CDC") claims to have invented the concepts of PEP and PrEP—publicly-available resources made clear that others had conceived of using antiretroviral treatment therapies, including Truvada, for PEP and PrEP. For this reason, Gilead strongly believes these patents are not valid and should not have been granted by the Patent and Trademark Office.

The CDC claims it conceived of the idea to use Truvada for PEP and PrEP by February 2006. By contrast, in November 2004, two prominent California-based HIV/AIDS organizations published guidelines that recommended administering combination antiretrovirals—including Truvada—to certain categories of "high risk" individuals before HIV exposure. These guidelines stated that Truvada could be used for prophylaxis, including PrEP, more than a year before the CDC filed patents claiming the exact same treatment.[9] As such, Truvada for PrEP was not a novel invention in February 2006, and the CDC's patents are therefore invalid.

Moreover, more than a year before CDC scientists claimed to have invented PEP and PrEP, the agency itself was aware of the use of Truvada for prophylaxis. In guidelines published in January 2005, the CDC explained that Truvada was the preferred drug for use in PEP. These guidelines encouraged the use of PEP "as soon as possible"—and no later than 72 hours—after exposure, recognizing that the sooner a patient exposed to HIV began taking Truvada, the more likely the drug would be to interrupt replication of the virus. Two individuals named as inventors on the CDC patents are listed as "Federal Consultants" on these guidelines.[10] This additional prior publication serves as further evidence that many claims included in the CDC patents—which also claim the use of Truvada for PEP—are invalid.

Finally, in 2004 and 2005, the CDC conducted surveys at Gay Pride events to document that gay men already were practicing PrEP with existing antiretroviral agents approved for HIV treatment.[11] This information demonstrates that others were using the technique before the CDC sought patents. Moreover, as this information was known to the CDC before its filing, the information should have been disclosed to the Patent Office.

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[9] *See* Greg Zekeres et al., Ctr. for HIV Identification, Prevention, & Treatment Servs., ANTICIPATING THE EFFICACY OF HIV PRE-EXPOSURE PROPHYLAXIS (PREP) AND THE NEEDS OF AT-RISK CALIFORNIANS (2004), *available at* http://www.uclaisap.org/assets/documents/PreP_Report_FINAL_11_1_04.pdf.

[10] *See* Ctrs. for Disease Control & Prevention, *Updated U.S. Public Health Service guidelines for the management of occupational exposures to HIV and recommendations for Postexposure Prophylaxis*, 54 Morbidity & Mortality Weekly Report, Sept. 30, 2005, at 1, *available at* https://www.cdc.gov/mmwr/PDF/rr/rr5409.pdf.

[11] *See* Scott E. Kellerman, *Knowledge and Use of HIV Pre-Exposure Prophylaxis Among Attendees of Minority Gay Pride Events, 2004,* 43 J. Acquired Immune Deficiency Syndromes 376 (2006).

Representative Chip Roy

1. *Can you explain the timeline of the research and development of Truvada, including the patent approval dates for Truvada as a treatment and as a preventative for HIV?*

Research and Development of Tenofovir Disoproxil Fumarate ("TDF")

Over more than a decade, Gilead invested hundreds of millions of dollars in the clinical development of the components of Truvada and their combination in one tablet. In so doing, Gilead shouldered the risk and expense of transforming the compounds that comprise Truvada into medicines used to treat and prevent HIV.

In 1991, Gilead licensed the rights to a portfolio of nucleotide compounds from the Rega Institute for Medical Research and the Institute of Organic Chemistry and Biochemistry. After nearly a decade of Gilead-led research and development, these nucleotides—including a compound called tenofovir—would go on to serve as the foundation of the company's innovative HIV treatment and prevention development program.

Although nucleotides were known to have notable antiviral activity, concerns regarding their toxicity reduced interest in licensing and developing them before Gilead took up the task. Indeed, before Gilead licensed the nucleotide portfolio in 1991, another major American pharmaceutical company licensed the compounds but abandoned efforts to develop them into an antiviral medication in light of concerns regarding their toxicity. Moreover, one of the nucleotides—tenofovir—could not be administered orally, which made its use as a drug to treat a chronic disease like HIV untenable.

Accordingly, in the early 1990s, Gilead began working to invent prodrugs that could be administered orally. Over the course of 18 months, Gilead synthesized hundreds of different prodrugs for the nucleotide adefovir, which were included in a patent application the company filed in 1994. Gilead ultimately developed these drugs into FDA-approved treatments for hepatitis B and other chronic diseases.

After selecting a prodrug of adefovir, Gilead began the selection process for another nucleotide active against HIV, ultimately choosing tenofovir. Gilead's discovery work then turned to the invention of a prodrug of tenofovir. During this process, Gilead screened more than 100 such drugs for toxicity and appropriate antiviral activity. Through this process, Gilead recognized that TDF was more bioavailable and safer than other tenofovir prodrugs and selected the drug for further development. Gilead sought a patent for TDF in 1997, which was ultimately granted and expired in 2017.

Following promising results in Gilead-sponsored pre-clinical and clinical trials, the company moved forward with bringing TDF to market as an HIV treatment therapy. After TDF was approved by the FDA in 2001, Gilead began marketing the drug for HIV treatment under the brand name Viread—ten years after the company licensed the nucleotide class of compounds and began its search for a life-saving HIV treatment drug.

Combining TDF with Emtricitabine ("FTC") to Create Truvada

In the early 2000s, HIV treatment required combination therapy, with the standard of care being the combination of two nucleoside reverse transcriptase inhibitors and a third agent from a separate class. With patients required to take three separate pills, each of which presented different potential side effects, these multi-tablet regimens presented complexity and

a risk of non-adherence, which reduced the efficacy of the treatments and could lead to viral resistance. Gilead developed Truvada as a fixed-dose combination pill, and then TDF-based single-tablet regimens ("STRs"), to encourage adherence and ultimately more effective HIV treatment.

Following the launch of Viread in 2001, providers commonly prescribed Viread in combination with Glaxo's Epivir (lamivudine or "3TC") and a third agent to treat HIV. Seeing an opportunity to reduce the number of pills a patient would be required to take each day, Gilead began searching for a compound to pair with TDF in order to create a combination pill that would ease this burden on patients.

Through these efforts, Gilead identified FTC, a compound discovered by researchers at Emory University and licensed to Triangle Pharmaceuticals. FTC was a potentially effective partner for TDF with a superior profile—longer half-life, increased potency, and less resistance—to 3TC. FTC was first synthesized in the early 1990s. After initial research demonstrated FTC's anti-HIV potency, Emory sought assistance from the private sector in funding the clinical development of FTC. These efforts were ultimately led by Triangle, which sponsored clinical trials in the early 2000s and sought FDA approval for FTC to be used to treat HIV in September 2002.

In January 2003, Gilead acquired Triangle, along with the rights to FTC, for more than $525 million, which reflected the value of the development work that already had been conducted by Triangle and its previous partners. After the acquisition, Gilead continued clinical studies to develop the compound for commercial use. As a result of all these efforts, in July 2003, the FDA approved FTC for use in combination with other antiretroviral agents for HIV treatment. Gilead has since marketed FTC under the brand name Emtriva. The basic patent on FTC, which was originally filed in 1991, was granted in 2004.

Even before the Triangle acquisition was finalized, Gilead had begun working on how to co-formulate the two compounds, TDF and FTC, to create Truvada. This led to the filing of a provisional patent application covering the combination in January 2003; the first patent to issue from that application was granted in 2013. Truvada was approved by the FDA in August 2004 as one of the first fixed-dose combination pills for HIV treatment.

Research and Development of Truvada for PrEP

As Gilead worked to develop Truvada, the company's research was primarily focused on developing more effective HIV treatment medications with fewer debilitating side effects than products then on the market. Even during this early period of development, however, it was clear to Gilead that tenofovir had potential prophylactic uses.

Most notably, prior to 1995, Gilead's former head of research and development, Norbert Bischofberger, led an effort to assist two NIH-funded studies conducted at the University of Washington. In addition to providing free tenofovir for use in the studies, Gilead helped design the study methodology, provided dosing guidance, and participated in analysis of the results. One such study—which demonstrated that tenofovir was effective as both a pre- and post-exposure prophylactic in response to "systemic" exposure to the virus in monkeys—was published in *Science* magazine in 1995, with Bischofberger credited as an author. The results of the second study—which demonstrated tenofovir's efficacy as a gel-based prophylactic in response to vaginal exposure to HIV in monkeys—were later presented at an antiviral meeting in Japan.

Based on this and other studies, and almost immediately after the approval of Viread for HIV treatment, researchers in 2002 proposed clinical studies in West Africa and Cambodia to demonstrate the efficacy of tenofovir in preventing new HIV infections. Gilead supported this research by providing free drug and assistance in study design.

Although the likelihood that tenofovir-based PrEP would prove effective was well established through these early studies, in the years that followed some in the HIV/AIDS community opposed further research regarding the use of antiretroviral medication for PrEP. During the early 2000s, investments in PrEP were viewed by some as undercutting vaccine research and public health campaigns focused on safe-sex practices, such as condom use. Similarly, the clinical studies proposed for West Africa and Cambodia to test the efficacy of PrEP therapies were accused of cultural insensitivity and failing to provide patients exposed to HIV with access to broad-scale treatment and other health care if PrEP therapies ultimately proved ineffective. Most of the human studies either did not launch or were terminated by 2004, after protests that questioned the ethics and motives of the research.

Mindful of these concerns, Gilead began working with public health authorities and others to support PrEP development efforts. In particular, after Truvada was approved for treatment, Gilead again provided the drug and other technical assistance to CDC to test the regimen in a monkey model of prevention. The CDC studies relied on a well-known model meant to replicate more closely exposure to HIV in humans. In 2007, based on the monkey study data, the CDC filed a patent application claiming the use of Truvada for PEP and for PrEP, which was granted in 2015. Several continuations of that patent have since been approved. (For the reasons cited in response to Representative Ocasio-Cortez's question #3, Gilead firmly believes the patents granted to the CDC are invalid.)

Around the same time as the CDC monkey study, a team of researchers began preparing for new human clinical trials in several countries, which were sponsored by the National Institutes of Health and the Bill and Melinda Gates Foundation. As before, Gilead supported the clinical trials by consulting and providing Truvada for patients enrolled in the trials. As a result of these efforts, Gilead scientists were credited as authors when the study results were published. A second clinical study conducted by the University of Washington was also funded by the Gates Foundation.

In 2012, Gilead submitted the results from these trials along with other data to the FDA to obtain approval for the use of Truvada for PrEP. Even following successful clinical trials, many participants in the public hearings convened by the FDA advocated against approval, again for reasons grounded in policy and ethics.[12] Ultimately, the FDA approved Truvada for PrEP in 2012.

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[12] *See* Press Release, AIDS Healthcare Foundation, 618 Doctors & Advocates Agree: "There is No Magic HIV Prevention Pill," Says AHF Ad (July 13, 2011), *available at* https://www.businesswire.com/news/home/20110713006684/en/618-Doctors-Advocates-Agree-%E2%80%9CThere-Magic-HIV; Josh Barro, *AIDS Group Wages Lonely Fight Against Pill to Prevent H.I.V.*, N.Y. Times (Nov. 16, 2014), https://www.nytimes.com/2014/11/17/upshot/aids-group-wages-lonely-fight-against-pill-to-prevent-hiv.html.

2. *How many patents exist on the drug?*

Gilead or Gilead-Licensed Patents on Components of Truvada and Their Use for HIV Treatment

There are no existing patents covering TDF. FTC is covered by U.S. Patent Nos. 6,642,245 (expiring May 4, 2021, claiming use of FTC to treat HIV infections) and 6,703,396 (expiring September 9, 2021, claiming FTC). Gilead has agreed to allow generic manufacturers to enter the market prior to the expiration of these patents.

Gilead Patents on Truvada and Its Use for HIV Treatment

Truvada is covered by U.S. Patent No. 8,592,397 (and its continuations 8,716,264, 9,457,036 and 9,744,181) (expiring January 14, 2024, and covering co-formulations of TDF and FTC). Gilead has agreed to allow generic manufacturers to enter the market prior to these patents' expiration.

Gilead Patents on the Use of Truvada for PEP or PrEP

Gilead has not separately patented the use of Truvada for PrEP. Its foundational patents on FTC, TDF and their combination cover all uses of the compounds, including treatment, PEP, and PrEP.

3. *Can you elaborate on the relationship between the patent that Gilead possesses and the CDC?*

CDC has no relationship to Gilead's patents and was not involved in the development of Truvada, FTC, or TDF. CDC's patent claims are directed to methods of treatment using Gilead's Truvada product for PEP (post-exposure prophylaxis) and PrEP (pre-exposure prophylaxis). The CDC patents were not filed until 2006—after Gilead brought Truvada to market and after scientists, doctors, and HIV/AIDS organizations practiced and recommended the idea of using combinations of antiretrovirals, such as Truvada, for PEP and PrEP. As such, these patents are not valid and should not have been granted by the Patent and Trademark Office.

4. *How large is the R&D arm of the company?*

As of May 2019, Gilead's research and development efforts were supported by 5,229 employees in 35 countries. At the end of 2018, the company's research and development pipeline included 119 active clinical studies, of which 41 were Phase III clinical trials. With respect to HIV in particular, as of the end of the most recent quarter, Gilead had 38 ongoing clinical trials focused on HIV treatment and prevention, 14 of which are Phase III trials.

In addition to this Gilead-led clinical research, the company completed 26 collaborations, partnerships, and strategic investments in 2018, reflecting a commitment to enabling the company to access new technologies and drug candidates with the potential to evolve care for people with life-threatening illnesses. In total, Gilead invested $3.5 billion in research and development in 2018. These investments reflect the company's ongoing commitment to expanding its drug development pipeline across a range of diseases to address areas of significant unmet medical need while maintaining the company's long-term growth.

5. *How long was the FDA drug approval process for Truvada?*

Prior to the launch of Truvada, each of the drug's component compounds—TDF and FTC—was approved by the FDA for use in combination with other drugs in treating HIV. Specifically, Gilead filed an Investigational New Drug ("IND") application for TDF on March 18, 1997. Gilead later sought approval of TDF on April 30, 2001, with the FDA approving the drug on October 26, 2001 pursuant to the FDA's Priority Review process. Before the company was acquired by Gilead, Triangle Pharmaceuticals filed an IND for FTC on August 20, 1997, and submitted an application for approval for the drug on September 3, 2002. Gilead acquired Triangle in January 2003, after which the FDA approved the drug for use in combination with other antiretroviral agents for HIV treatment on July 2, 2003.

Gilead filed an IND for Truvada on July 2, 2003, and sought approval from the FDA of the use of Truvada to treat HIV on March 11, 2004. Gilead's application was designated for consideration under the FDA's Priority Review process, which is reserved for drugs that, if approved, would offer significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications. The FDA granted Gilead's application and approved Truvada for use in treating HIV on August 2, 2004. Finally, Gilead submitted an application for FDA approval of Truvada for PrEP on December 9, 2011. The FDA approved Gilead's application on July 16, 2012.

6. *At the time of the development of Truvada, how many drug treatments for HIV existed?*

The FDA approved the use of Truvada as a fixed-dose combination treatment for use in combination with other antiretroviral drugs to HIV on August 2, 2004. On the same day, the FDA approved a second combination treatment, which was itself a combination of two antiretroviral therapies previously approved by the FDA, for the use in treating HIV in combination with other antiretroviral drugs.

Prior to August 2004, the FDA approved 2 fixed-dose combination treatments, and 21 other new compounds for use in combination with other drugs to treat chronic HIV. As noted above, these included each of the components of Truvada—TDF and FTC. These previously approved compounds are identified, along with the dates on which they were approved for use in treating HIV, in the chart below.

Compounds Approved by the FDA for the Treatment of HIV
On or Before August 2, 2004

Compound	Date of FDA Approval
Truvada (TDF/FTC)	August 2, 2004
Epzicom (ABC/3TC)	August 2, 2004
Fosamprenavir Calcium	October 20, 2003
Emtricitabine (FTC)	July 2, 2003
Atazanavir Sulfate	June 20, 2003
Enfuvirtide	March 13, 2003
Tenofovir Disoproxil Fumarate (TDF)	October 26, 2001
Trizivir (ABC/3TC/AZT)	November 14, 2000
Didanosine EC	October 31, 2000
Lopinavir/Ritonavir	September 15, 2000
Amprenavir	April 15, 1999
Abacavir Sulfate (ABC)	December 17, 1998
Efavirenz	September 17, 1998
Combivir (3TC/AZT)	September 26, 1997
Delavirdine	April 4, 1997
Nelfinavir	March 14, 1997
Nevirapine	June 21, 1996
Indinavir	March 13, 1996
Ritonavir	March 1, 1996
Saquinavir	December 6, 1995
Lamivudine (3TC)	November 20, 1995
Stavudine	June 24, 1994
Zalcitabine	June 19, 1992
Didanosine	October 9, 1991
Zidovudine (AZT)	March 19, 1987

7. *What development and market factors have led to the price of Truvada in other countries (some $8.00) to be lower than the cost of the U.S. price (roughly $2,100)?*

The principal factor that has led Truvada to be sold at a lower price in developed countries outside of the United States has been the marketing and sale of generic TDF-FTC, which became available in Australia and the European Union starting in 2017. Gilead has agreed to permit the entry of the first generic TDF-FTC in the United States on September 30, 2020, approximately one year before what is required under Gilead's domestic FTC patent and more than three years before expiration of other patents covering Truvada.

In addition to the patent-related issues described above, several other factors contribute to the differential pricing of Truvada across public and private payers globally. These factors include a particular patient population's disease burden, approved indications of the drug (i.e., treatment, prevention, or both), the government's willingness and ability to pay, market dynamics, and the structure of insurance markets specifically related to drug delivery. Finally, through the company's Access Program, Gilead has also permitted generic companies to provide TDF-FTC at very low cost to people in developing countries that would otherwise not be able to obtain these medicines (including many countries in Africa).

8. *Roughly how many individuals in the U.S. pay the full $2,100*[13] *for the drug? Is the drug covered through insurance? Medicaid? Medicare?*

Whether used to treat HIV or for PrEP, Truvada enjoys wide coverage on both commercial and public insurance plans in the United States. In total, as of June 2019, 99.7% of individuals with health insurance have a plan that covers Truvada. In particular, 100% of individuals with State Medicaid insurance have Truvada coverage, with more than 99% of individuals on managed Medicaid having a plan that covers the drug. Similarly, 99.8% of individuals on commercial insurance are on plans that include Truvada on their formularies, with roughly 99.6% of individuals on Medicare Part D plans covering the drug. Although Truvada is nearly universally included on insurer formularies, some insurers require prior approval before agreeing to cover the drug. Overall, approximately 5% of individuals are on plans that include such a prior approval requirement for Truvada, with 2% of individuals on plans that specifically require prior approval for Truvada for PrEP.

Due to the drug's broad coverage under both public and private insurance plans, as well as Gilead's copay assistance and other patient assistance programs, few patients who are prescribed Truvada encounter significant out-of-pocket costs. Gilead does not actively track out-of-pocket costs for all individuals who obtain Truvada for treatment or for PrEP. According to the CDC, when taking Gilead's patient assistance programs into account, less than 1% of the estimated number of Americans at high risk for contracting HIV have an entirely unmet need for financial coverage for Truvada for PrEP.[14]

[13] Contrary to some media reports, the current list price for Truvada, whether taken for treatment or for PrEP, is $21,388 per year. Excluding rebates offered to certain payers, this equates to a monthly cost of $1,780 for the drug.

[14] Dawn K. Smith et al., *Estimated coverage to address financial barriers to HIV preexposure prophylaxis among persons with indications for its use, United States, 2015*, 76 J. Acquired Immune Deficiency Syndromes 475 (2017).