Yale *Global Health Justice Partnership*
A PROGRAM OF YALE LAW SCHOOL AND THE YALE SCHOOL OF PUBLIC HEALTH

May 16, 2019

To:
The Honorable Elijah Cummings
Chairman, House Committee on Oversight and Reform
The Honorable Jim Jordan
Ranking Member, House Committee on Oversight and Reform

From:
Amy Kapczynski, Faculty Co-Director, Global Health Justice Partnership
Christopher Morten, Fellow, Global Health Justice Partnership

Re:
May 16, 2019 Hearing on "HIV Prevention Drug: Billions in Corporate Profits after Millions in Taxpayer Investments"

Dear Chairman Cummings, Ranking Member Jordan, and members of the House Committee on Oversight and Reform:

We write on behalf of the Yale Global Health Justice Partnership (GHJP). GHJP is a program hosted jointly by Yale Law School and Yale School of Public Health that tackles contemporary problems at the interface of global health, human rights, and social justice. Among other projects, GHJP undertakes research and advocacy to ensure more integrity and transparency in clinical research and to bring about a more just system for the development and distribution of medicines.

Amy Kapczynski is Faculty Co-Director of GHJP and a Professor of Law at Yale Law School. She teaches and researches intellectual property law, international law, and global health. She is an expert on the question of how to promote greater access to medicines and has studied, for over 15 years, the legal determinants of high prices for prescription drugs in the United States. Her scholarship on prescription drugs has been published in high-profile journals, including the *Journal of the American Medical Association,* the *New England Journal of Medicine*, and the *Yale Law Journal*.

Christopher Morten is a Fellow at GHJP and a Lecturer at Yale Law School, where he teaches in the Media Freedom and Information Access Clinic and litigates and researches matters promoting greater access to information on prescription drugs. He is a licensed patent attorney and holds a Ph.D. in organic chemistry.

P.O. BOX 208215, NEW HAVEN, CONNECTICUT 06520-8215 • FACIMILIE 203 436-9397
COURIER ADDRESS 127 WALL STREET, NEW HAVEN, CONNECTICUT 06511 • HEALTH.JUSTICE@YALE.EDU
WWW.LAW.YALE.EDU/GHJP

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We thank the Committee for holding a hearing on the issue of the unreasonable prices charged by Gilead Sciences, Inc. (Gilead) for an HIV prevention drug known as Truvada, which is used for pre-exposure prophylaxis (PrEP). We understand that the hearing will examine the taxpayer funding that led to approval by the Food and Drug Administration (FDA) of Truvada for PrEP and will address the issue of whether the public is receiving an appropriate return on its investment. We respectfully submit this letter to shed further light on these issues.

Gilead does indeed charge an unreasonable price for Truvada, at least in the United States. In the United States, Truvada is very expensive: Gilead charges over $2,000 per month average wholesale price, almost $70 per pill.[1] But Truvada does not need to be expensive: it costs less than $6 per month to manufacture, or less than 20 cents per pill.[2] The cost of Truvada creates a barrier to access. As the testimony of Dr. Robert Grant highlights, only 1 in 10 people who would benefit from PrEP are receiving it in the United States.[3]

The price that Gilead charges for Truvada is particularly galling in view of the fact that the public, and not Gilead, paid for the research that first discovered, and then proved, that Truvada is effective as HIV PrEP. This is consistent with a broader fact of pharmaceutical development and research: the American public funds a great deal of research that is essential to pharmaceutical development, and in particular for breakthrough drugs. A 2018 study concluded that funding from the National Institutes of Health (NIH) "contributed to published research associated with every one of the 210 new drugs approved by the Food and Drug Administration from 2010–2016. Collectively, this research involved >200,000 years of grant funding totaling more than $100 billion."[4] A separate 2015 study showed that transformative drugs—"pharmaceuticals that are both innovative and have groundbreaking effects on patient care"—are disproportionately created with public money and concluded that "many of the key insights behind these transformative products emerged in publicly funded basic research in university settings and were then further developed through collaboration between public and private

[1] The Average Wholesale Price (AWP) for Truvada was described as $2,011 per 30-day supply in a recent report. *See*: Table 17, Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.

[2] Hill AM and Pozniak AL. "How can we achieve universal access to low-cost treatment for HIV?" J Virus Erad. 2016 Oct 5;2(4):193-197.

[3] Testimony of Robert M. Grant dated May 16, 2019. https://docs.house.gov/meetings/GO/GO00/20190516/109486/HHRG-116-GO00-Wstate-GrantR-20190516-U1.pdf.

[4] Cleary EG et al., "Contribution of NIH funding to new drug approvals 2010–2016," Proceedings of the National Academy of Sciences Mar 2018, 115 (10) 2329-2334; DOI: 10.1073/pnas.1715368115.

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entities."[5] Yet pharmaceutical companies make no concessions to the public in their pricing of these medicines, forcing taxpayers to pay twice: first with their tax dollars invested in drug discovery and then again with their tax dollars (for public insurance programs like Medicaid), private insurance premiums, and individual payments at the pharmacy.

While brand-name pharmaceutical companies frequently claim that the very high drug prices charged to Americans are necessary to support the research and development necessary to create new prescription drugs, this claim is questionable. For example, a recent study of the 10 largest U.S.-based pharmaceutical companies that generate more than half of their revenues from prescription drugs showed they spent an average of only 22% of their revenues on R&D in 2017.[6] Of the 10 companies highlighted in the study, Gilead spent the least: only about 14% of its revenues went to R&D.[7]

The Truvada example is notable for the significance of the government research in development of the drug. As Dr. Robert Grant's testimony notes, "[t]he US Government is by far the majority funder of PrEP research."[8]

First, government-funded scientists, not Gilead, conducted the early preclinical testing (animal studies) that first showed the promise of Truvada as HIV PrEP. Specifically, a team of scientists at the Centers for Disease Control and Prevention (CDC) led by Dr. J. Gerardo García-Lerma performed experiments in rhesus macaques (a type of monkey) with the same two active pharmaceutical ingredients found in Truvada and discovered that the two-drug combination effectively prevented HIV infection. In 2008, these scientists published a paper disclosing their results: "full protection against repeated exposures [to HIV] by daily PrEP [with the active ingredients found in Truvada] is possible in a primate model."[9] Before this, Truvada was known only as a method of treating HIV in people who were already infected with the virus.

Then, after CDC scientists conducted these critical early studies that first established the promise of Truvada as HIV PrEP, other entities conducted testing in humans (clinical studies) to establish that Truvada PrEP is indeed safe and effective. Again, public research dollars funded

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[5] Kesselheim AS, Tan YT, Avorn J, "The Roles Of Academia, Rare Diseases, And Repurposing In The Development Of The Most Transformative Drugs," Health Affairs 34(2) (2015), https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2014.1038.

[6] Florko N, "A new study sparks a war of words over the drug industry's commitment to research," STAT News May 14, 2019, https://www.statnews.com/2019/05/14/war-of-words-over-pharma-commitment-to-research/.

[7] *Id.*

[8] Testimony of Robert M. Grant dated May 16, 2019. https://docs.house.gov/meetings/GO/GO00/20190516/109486/HHRG-116-GO00-Wstate-GrantR-20190516-U1.pdf.

[9] J. Gerardo García-Lerma et al., Prevention of Rectal SHIV Transmission in Macaques by Daily or Intermittent Prophylaxis with Emtricitabine and Tenofovir, 5 PLoS Medicine e28 (2008).

the research, not Gilead. When companies wish to market a drug for a particular method of use, they must get approval from the FDA. To gain approval, companies submit evidence to the FDA and identify the most important studies supporting the safety and efficacy of the use. To gain approval from the FDA to market Truvada for use as PrEP, Gilead relied primarily on two studies, iPrEx and Partners PrEP.[10] Gilead did not sponsor or fund either of these studies essential for FDA approval. Instead, the iPrEx study was sponsored and funded by an agency of the federal government, the NIH, through its Division of AIDS.[11] The NIH spent approximately $50 million in public funds on the iPrEx study.[12] The Partners PrEP study was sponsored by the University of Washington[13] and was funded by the Bill and Melinda Gates Foundation.[14] According to the FDA, this trial "demonstrated that Truvada was effective in men and women" for prevention of HIV.[15]

As the May 14, 2019, memorandum of the Democratic Members of the Committee points out, the CDC has filed at least seven patents in the U.S. and abroad on HIV PrEP. The existence of these patents corroborates the point that it was the CDC, not Gilead, that invented the method of preventing HIV in HIV-negative individuals by giving Truvada or a similar drug once a day. We at GHJP have analyzed the CDC's U.S. patents in some detail and have concluded, based on our analysis, that the patents appear to be valid, enforceable, and infringed by Gilead's sale of Truvada as HIV PrEP.[16]

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[10] *See* Prescribing information for TRUVADA® (emtricitabine and tenofovir disoproxil fumarate) tablets dated 05/2018 at sections 14.3, 14.4. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021752s055lbl.pdf. *See also* Supplemental Submission 30 ("PrEP Indication") for NDA 21752 (Truvada), US FDA. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/021752Orig1s030SumR.pdf.

[11] Supplemental Submission 30 ("PrEP Indication") for NDA 21752 (Truvada), US FDA, at 4. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/021752Orig1s030SumR.pdf. *See also* testimony of Dr. Robert Grant, https://docs.house.gov/meetings/GO/GO00/20190516/109486/HHRG-116-GO00-Wstate-GrantR-20190516-U1.pdf.

[12] JB Krellenstein, "Taxpayer Funded Development of Truvada as PrEP." https://breakthepatent.org/wp-content/uploads/2019/05/Truvada-RD-PrEP-Taxpayer-Cost-v0.2.pdf

[13] Supplemental Submission 30 ("PrEP Indication") for NDA 21752 (Truvada), US FDA, at 5. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/021752Orig1s030SumR.pdf.

[14] Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med. 2012;367(5):399-410.

[15] Supplemental Submission 30 ("PrEP Indication") for NDA 21752 (Truvada), US FDA, at 5. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/021752Orig1s030SumR.pdf.

[16] Summary of GHJP Statement on CDC's Patents for PrEP: https://law.yale.edu/system/files/area/center/ghjp/documents/ghjp2-pagestatement.pdf.
Full Statement of GHJP on CDC's Patents for PrEP: https://law.yale.edu/system/files/area/center/ghjp/documents/ghjpmortenstatement.pdf.

In the United States, every patent application is examined by a patent examiner to determine whether it should issue as a patent and take legal force. The patent examiner determines whether the inventions claimed within a patent application are novel (new), nonobvious, adequately enabled, adequately described, and clearly and distinctly claimed. As explained in GHJP's statement dated March 12, 2019, the patent examiner at the United States Patent and Trademark Office (USPTO) examined the claims of the CDC's patent applications and determined that they meet the conditions and requirements of patentability under U.S. law. The patent examiner concluded that CDC's results were "significant" and "would not have been expected in view" of the medical literature that the examiner reviewed.[17] The patent examiner also observed that, at the time the CDC filed its first patent application, other researchers had tried but failed to develop a once-daily pill to prevent HIV infection in HIV-negative people.[18] In addition, a division of the global pharmaceutical company Mylan challenged the validity of the CDC's European patent in an intensive, multi-year inter partes procedure known as an "opposition," but the European Patent Office (EPO) concluded that the CDC should keep its patent.[19] After this unsuccessful challenge, Mylan agreed to pay a royalty to the CDC for use of its patents.[20] The fact that the CDC holds patents around the world on HIV PrEP is further evidence that it was the CDC, and not Gilead, that invented HIV PrEP.[21]

Gilead has known about the CDC's patents for years.[22] For example, in a statement filed with the Securities and Exchange Commission and dated February 27, 2017, Gilead disclosed that "[w]e have been in contact with the U.S. Department of Health and Human Services about the scope and relevance of" U.S. Patent No. 9,044,509, the first of the CDC's U.S. patents.[23]

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[17] Full Statement of GHJP on CDC's Patents for PrEP: https://law.yale.edu/system/files/area/center/ghjp/documents/ghjpmortenstatement.pdf.

[18] *Id.*

[19] *Id.*

[20] Ed Silverman, "AIDS activists skewer CDC for conflicting stance on collecting HIV drug royalties," STAT News April 10, 2010. https://www.statnews.com/pharmalot/2019/04/10/aids-cdc-hiv-patents-royalties/.

[21] We at GHJP are generally supportive of Congressional and other efforts to combat patent "evergreening." We have serious concerns about the value that method of treatment patents like the CDC's patents for PrEP (and still more other "secondary" patents such as patents on polymorphic forms, new formulations, etc.) provide to the public. But under current law, such patents are both valid and common. Indeed, they are regularly used by the pharmaceutical industry to artificially extend patent protection on expensive brand name drug products, delay generic competition, and keep prices high. Under these circumstances we see no valid argument that government should not use its own method of treatment patents to promote fair prices.

[22] Madison Alder, "HIV Pill Patent Gives Trump Team Leverage in Gilead Price Talks," Bloomberg Law, April 12, 2019. https://www.bloomberglaw.com/document/X4EJSVUG000000?bna_news_filter=health-law-and-business&jcsearch=BNA%252000000016a0c97dcf2a97b9c9f73c30002#jcite.

[23] 2016 Form 10-K of Gilead Sciences, Inc. https://www.sec.gov/Archives/edgar/data/882095/000088209517000006/a2016form10-k.htm.

Gilead acknowledged in that statement that "[o]ur success depends in large part on our ability to operate without infringing upon the patents or other proprietary rights of third parties."[24]

Yet Gilead now contends that it should not be held liable for infringing the CDC's patents because the CDC's patents are invalid. One argument Gilead now makes is that Truvada was already being used by doctors and patients "off label" (meaning in a way not yet approved by the FDA) to prevent HIV infection in HIV-negative people before the CDC patent application was filed in 2006.[25] Despite Gilead's suggestion, we have not seen any evidence that this is true – not in the medical literature and not in the records developed before the USPTO and EPO that we have reviewed. In fact, our review of the medical literature indicates that even as of 2010, years after the CDC filed its patent applications, it was major news that Truvada worked as HIV PrEP. In 2010, a team of researchers led by Dr. Robert Grant published a high-profile article in the *New England Journal of Medicine* on Truvada PrEP. Dr. Grant's article was important because it was the first to conclude that "[o]ral FTC–TDF [the active ingredients in Truvada] provided protection against the acquisition of HIV infection" among the people in the trial.[26] Dr. Grant's article does not mention doctors using Truvada off label as HIV PrEP. Instead, Dr. Grant's article credits the CDC researchers as having helped to pave the way for his study by showing "[t]he protective activity of FTC and TDF" (the active ingredients) in Truvada in their monkey studies (citing the CDC researchers' 2008 article).[27] Similarly, Dr. Grant's testimony to this Committee acknowledges that when he began his clinical investigation, "PrEP regimen selection was guided by research conducted by scientists at the CDC who demonstrated that adding emtricitabine to a tenofovir regimen increased protection."[28] Dr. Grant also states that "[t]he CDC work nucleated my decision to use a combination tablet rather than tenofovir alone."[29]

Gilead also now contends that it contributed to the invention of Truvada PrEP. A spokesperson for Gilead stated that the CDC's patents "do not reflect the contributions of Gilead scientists, who collaborated with the CDC to design the monkey studies that underlie the

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[24] *Id.*

[25] Christopher Rowland, "An HIV treatment cost taxpayers millions. The government patented it. But a pharma giant is making billions," Washington Post, March 26, 2019. https://www.washingtonpost.com/business/economy/pharma-giant-profits-from-hiv-treatment-funded-by-taxpayers-and-patented-by-the-government/2019/03/26/cee5afb4-40fc-11e9-9361-301ffb5bd5e6_story.html?utm_term=.db5fd5c147e0.

[26] Grant RM et al., "Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men," New Engl. J. Med. 2010; 363:2587-2599. https://www.nejm.org/doi/full/10.1056/NEJMoa1011205.

[27] *Id.*

[28] Testimony of Dr. Robert Grant, https://docs.house.gov/meetings/GO/GO00/20190516/109486/HHRG-116-GO00-Wstate-GrantR-20190516-U1.pdf.

[29] *Id.*

patents."[30] A May 14, 2019 press release from Gilead alleges that "[t]he government did not invent PrEP, Truvada or Truvada for PrEP®" and that Gilead "support[ed] the clinical trials that led to the approval of Truvada for PrEP."[31] Again, despite Gilead's contentions, there is nothing we have seen to support the notion that Gilead employees contributed to the design of the CDC's monkey studies or otherwise co-invented Truvada PrEP. The CDC's patents do not mention any inventive contribution by Gilead. The 2008 paper published by the CDC researchers thanks Gilead for providing drug samples but describes no inventive contribution from Gilead.[32] As to later clinical trials of Truvada PrEP, Dr. Grant's testimony to this Committee explains that "Gilead Sciences did not provide leadership, innovation, or funding for these projects; Gilead's role was limited to donating study medication and placebos."[33]

While we are not aware of any evidence that the CDC's patents are invalid or that Gilead contributed to the invention of Truvada PrEP, we have seen evidence that Gilead has been infringing the CDC's patents by selling Truvada for use as PrEP.[34] Our March 12, 2019, statement explains that Gilead appears to instruct doctors and patients to infringe at least one claim of the CDC's patents.[35] Infringement of a patent claim can create liability, including potential money damages owed to the patent owner. Should the CDC and the U.S. government decide to enforce its patents, the CDC could possibly collect money from Gilead that could be used for public health purposes, including creating a National Access Plan for PrEP and improving care for people with HIV.[36] The CDC and the U.S. government could also use the CDC's patents as leverage to demand that Gilead reduce the prices that it charges for Truvada in

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[30] Christopher Rowland, "An HIV treatment cost taxpayers millions. The government patented it. But a pharma giant is making billions," Washington Post, March 26, 2019. https://www.washingtonpost.com/business/economy/pharma-giant-profits-from-hiv-treatment-funded-by-taxpayers-and-patented-by-the-government/2019/03/26/cee5afb4-40fc-11e9-9361-301ffb5bd5e6_story.html?utm_term=.db5fd5c147e0.

[31] https://www.gilead.com/news-and-press/company-statements/gilead--sciences--statement--on--inaccurate--reporting--on--truvada.

[32] J. Gerardo García-Lerma et al., Prevention of Rectal SHIV Transmission in Macaques by Daily or Intermittent Prophylaxis with Emtricitabine and Tenofovir, 5 PLoS Medicine e28 (2008).

[33] Testimony of Dr. Robert Grant, https://docs.house.gov/meetings/GO/GO00/20190516/109486/HHRG-116-GO00-Wstate-GrantR-20190516-U1.pdf.

[34] Full Statement of GHJP on CDC's Patents for PrEP: https://law.yale.edu/system/files/area/center/ghjp/documents/ghjpmortenstatement.pdf. As noted above, we know from Gilead's SEC filings that Gilead has known about the CDC's patents for years, and thus we do not believe that Gilead could claim lack of knowledge of the CDC's patents as a defense to infringement.

[35] *Id.*

[36] GHJP's March 27, 2019 press release: https://law.yale.edu/yls-today/news/ghjp-joins-prep4all-calling-cdc-use-its-patents-prep.
Demand letter from 40+ civil society groups to CDC and HHS: https://breakthepatent.org/wp-content/uploads/2019/04/PrEP4All-CDC-Demands-Letter.pdf.

the U.S. and work with public health agencies at the federal, state, and local level to improve prevention and treatment of HIV around the country.[37]

The CDC's patents for PrEP are just one of many tools that the federal government has to bring down the price of Truvada. Because the patents that Gilead currently uses to block generic competitors from the market were created with federal grant money,[38] the federal government could exercise its paid-up license and march-in rights under the Bayh-Dole Act to accelerate generic competition and bring prices down. The federal government holds additional rights in all U.S. patents (not only those created with federal grant money) through a longstanding federal statutory provision known as 28 U.S.C. § 1498.[39] Under existing law, the federal government could exercise these rights to promote competition and bring down prices for hundreds of very expensive brand-name drugs that Americans currently struggle to afford.

We thank the Committee for holding this hearing and for its consideration of this letter.

Sincerely,

Amy Kapczynski, J.D., M.A., M.Phil.
Professor of Law, Yale Law School
Faculty Co-Director, Global Health Justice Partnership

Christopher Morten, J.D., Ph.D.
Fellow, Global Health Justice Partnership
Registered Patent Attorney (Reg. No. 69,974)

[37] *Id.*

[38] *See* U.S. Patent Nos. 6,642,245 and 6,703,396; *see also* "A NATIONAL ACTION PLAN FOR UNIVERSAL ACCESS TO HIV PRE-EXPOSURE PROPHYLAXIS (PrEP) IN THE UNITED STATES." https://www.poz.com/pdfs/national-action-plan-prep-2018.pdf.

[39] *See* Kapczynski A & Kesselheim AS, "Why 'Government Patent Use' To Lower Drug Costs Won't Stifle Innovation," Health Affairs Blog July 28, 2016. https://www.healthaffairs.org/do/10.1377/hblog20160728.055969/full/; *see also* "A NATIONAL ACTION PLAN FOR UNIVERSAL ACCESS TO HIV PRE-EXPOSURE PROPHYLAXIS (PrEP) IN THE UNITED STATES." https://www.poz.com/pdfs/national-action-plan-prep-2018.pdf.