UNITED STATES DISTRICT COURT

FOR THE MIDDLE DISTICT OF NORTH CAROLINA

ANTONIO GEE, BARRY WILLIAMS, DEWEY GOOLSBY, DONNA L. FRANCIS, DONNIE L. JONES, ELIZABETH SCOGGINS, FERNANDO SAMUDIO, GAYE K. BENTON, GERALD FEWELL, JACQUELINE SMITH, JAMES A. FARLAND, JOSEPH G. BRISSON, JOSEPHINE PORTER, KIMBERLY S. JONES, LAVITA STANCIL, LINDA BLACKWELL, LYNWOOD MATTHEWS, MILDRED BATTISTE, MIRIAM M. EPPERSON, NORMAN R. BURWELL, PAMELA V. GBALAH, PATRICIA WALKER, REGGIE ERIC BRIGGS, REGINA TAYLOR, ROBERT TIMOTHY CARRINGTON, ROBERT I. WALKER, ROBERT LYNN WILLIAMSON, ROSEMARY WHELESS, RUTHIE HATCHER, SHANETTA N. HUNTER, SHELIA PINKARD, SONJA LIVINGSTON, STEPHEN M. YOUNG, TYRONE BROWN, VANESSA FULWILEY, VERONICA ANGELA MCCULLOUGH, AND WILLIAM T. BLUE,

Plaintiffs,

v.

GILEAD SCIENCES, INC.,

Defendant.

No. _____

COMPLAINT FOR DAMAGES

JURY TRIAL DEMANDED

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Plaintiffs bring this civil action for damages against Defendant Gilead Sciences, Inc. ("Gilead" or "Defendant"). Based on the investigation of counsel, Plaintiffs allege on information and belief as follows:

I. NATURE OF THE ACTION

1. This action arises out of injuries Plaintiffs sustained as a result of ingesting one or more of the prescription drugs Viread, Truvada, Atripla, Complera, and Stribild, which are manufactured and marketed by Gilead for the treatment of Human Immunodeficiency Virus-1 ("HIV") infection.[1]

2. Gilead designed each of the drugs to contain a form of the compound tenofovir that Gilead knew was toxic to patients' kidneys and bones. Tenofovir is a nucleotide analogue reverse transcriptase inhibitor ("NRTI"), one of the classes of antiretroviral drugs used to treat HIV. NRTIs work by blocking an enzyme HIV needs to replicate. Gilead did not discover tenofovir. Scientists in Europe discovered tenofovir in the 1980s, and though the anti-HIV properties of tenofovir were promising, it had a downside: it cannot not be administered effectively by mouth.

3. Because an intravenous tenofovir formulation had little sales potential, Gilead developed a form of tenofovir, tenofovir disoproxil, which can be taken orally.[2] The fumaric acid salt of tenofovir disoproxil is tenofovir disoproxil fumarate ("TDF"). When a patient takes a pill containing TDF, the patient's body converts TDF into tenofovir.

[1] Viread is also indicated to treat Hepatitis B. And Truvada is also indicated for use in combination with safe sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.

[2] Tenofovir disoproxil is a prodrug form of tenofovir. Prodrugs are pharmacologically inactive compounds that can be more efficiently absorbed into the bloodstream and then converted into the active form of the drug within the body.

Although TDF can be taken by mouth, a high dose of 300 mg is typically required to achieve the desired therapeutic effect.

4. Gilead designed TDF 300 mg to be an active ingredient in five drugs that are approved to treat HIV: Viread (TDF 300 mg tablets), approved October 26, 2001; Truvada (TDF 300 mg/emtricitabine 200 mg tablets), approved August 2, 2004; Atripla (TDF 300 mg/emtricitabine 200 mg/efavirenz 600 mg tablets), approved July 12, 2006; Complera (TDF 300 mg/emtricitabine 200 mg/rilpivirine 25 mg tablets), approved August 10, 2011; and Stribild (TDF 300 mg/emtricitabine 200 mg/elvitegravir 150 mg/cobicistat 150 mg tablets), approved August 27, 2012 (collectively, these are the "TDF Drugs").

5. Before Gilead began selling its first TDF Drug, Viread, in 2001, Gilead knew that TDF posed a safety risk to patients' kidneys and bones. Gilead knew that two of its other antiviral drugs with structures similar to tenofovir, cidofovir and adefovir dipivoxil, had been highly nephrotoxic (i.e., toxic to kidneys) and that preclinical data for TDF showed that it could cause significant kidney and bone damage. Gilead also knew that the relatively high dose of TDF created a greater risk of toxic effects, and that bone and kidney toxicities were even more likely to be seen with long-term use of TDF for the treatment of a virus that, for the foreseeable future, has no cure.

6. Gilead's knowledge of the toxic effects of TDF only grew as patients began treatment with and were injured by each successive TDF product. By the time Gilead designed Stribild, it had ten years' worth of cumulative evidence that TDF injured patients' kidneys and bones.

7. Gilead also knew, before it obtained approval to market Viread and Gilead's subsequent TDF Drugs, that it had discovered a safer tenofovir prodrug, tenofovir alafenamide fumarate ("TAF"). TAF is absorbed into the cells HIV targets much more efficiently than TDF. As a result, TAF can be administered at a dramatically reduced dose compared to TDF, but still achieve the same or higher concentrations of active tenofovir in

the target cells. Because TAF can be administered at a much lower dose than TDF, its use is associated with less toxicity and fewer side effects. A 25 mg dose of TAF achieves the same therapeutic effect as a 300 mg dose of TDF, with a better safety profile. Despite knowing that TAF could be given at a much lower, safer dose, Gilead designed Viread, Truvada, Atripla, Complera, and Stribild to contain TDF rather than safer TAF.

8. Falsely claiming that TAF was not different enough from TDF, Gilead abruptly shelved its TAF design in 2004. However, as John Milligan, Gilead's President and Chief Executive Officer, later admitted to investment analysts, the real reason Gilead abandoned the TAF design was that TAF was *too different* from TDF. Once Gilead's first TDF product, Viread, was on the market, Gilead did not want to hurt TDF sales by admitting that its TDF-based products are unreasonably and unnecessarily unsafe.

9. It was crucial at that time for Gilead to increase Viread sales, which comprised 53% of Gilead's total product sales in 2002, and 68% of Gilead's total product sales in 2003. Gilead was so desperate to expand Viread sales that when promoting the drug to doctors, it called Viread a "miracle drug" with "no toxicities." Gilead did not tell doctors the facts: that Viread posed significant risks to patients' kidneys and bones.

10. In addition, Gilead knew that by withholding the safer TAF design, it could extend the longevity of its HIV drug franchise and make billions two times over: first, with TDF medications until TDF patent expiration, which would begin by no later than 2018, and second, with TAF medications until TAF patent expiration as late as 2032. Only once Gilead realized billions in sales through most of the TDF patent life did it seek to market safer TAF-based versions of its HIV medications.

11. Finally, in 2015, Gilead began selling the first of its TAF-designed medicines and convinced doctors to switch their patients from TDF-based to TAF-based regimens by demonstrating TAF's superior safety profile over TDF with respect to kidney and bone

toxicity—the very benefits that Gilead could have and should have incorporated into its prior product designs but withheld from doctors and patients for over a decade.

12. Gilead also made Stribild even more dangerous to Plaintiffs when it designed the drug to include cobicistat in combination with 300 mg TDF. Cobicistat is a pharmacoenhancer or "booster" that inhibits the breakdown of elvitegravir, another active ingredient in Stribild. Cobicistat allows elvitegravir to persist in the patient's system long enough to permit once-daily dosing.

13. Gilead knew years before it developed Stribild that: (a) higher tenofovir concentrations in patients' blood, as opposed to the target cells, endangers the kidneys; (b) tenofovir concentrations in patients' blood increase significantly when patients take tenofovir with a booster; and (c) TDF-associated renal toxicity occurs more frequently in patients taking TDF as part of a boosted regimen.

14. When Gilead developed its first TAF-based antiviral product, Genvoya—which is Stribild with TAF in place of TDF—Gilead reduced the dose of TAF from 25 mg to 10 mg to account for the fact that cobicistat significantly increases tenofovir concentrations. Gilead knew to reduce the dose of TAF in Genvoya before it submitted Stribild to the FDA for marketing approval. Despite this knowledge, Gilead did not reduce the dose of TDF when it designed Stribild. Stribild is even more toxic to patients' kidneys and bones than Gilead's other TDF-based products.

15. In addition to withholding safer designs, Gilead failed to adequately warn physicians and patients about the risks and safe use of TDF. Gilead provided only the weakest, inadequate warnings to doctors and patients about the need for frequent monitoring of all patients for TDF-associated kidney and bone damage—preventing doctors from detecting early signs of TDF toxicity.

16. Gilead provides stronger monitoring warnings to physicians and patients in the European Union (EU) than it does in the United States for the exact same TDF products.

Contrary to its U.S. labeling, Gilead has consistently recommended, since the approval of its first TDF Drug in the EU, that doctors in the EU monitor all TDF Drug patients for multiple markers of TDF toxicity on a frequent, specified schedule. There is no scientific or medical rationale for these differences. Gilead was more concerned with increasing or maintaining crucial U.S. sales than it was in safeguarding patients from the known risks of TDF.

17. Gilead could have strengthened the warnings in its U.S. labels at any time, including before FDA approval for all TDF Drugs and after FDA approval for Viread, Truvada, Atripla, and Complera. After August 2008 through July 2012, Gilead could have unilaterally strengthened the warnings in its TDF Drug labels after approval based on: increasing evidence that patients with and without preexisting risk factors were experiencing adverse effects with a frequency and severity greater than reported in Gilead's Viread clinical trials; expanding evidence that all patients are at risk for TDF-induced nephrotoxicity; and Gilead's own determinations to give stronger warnings regarding the exact same TDF Drugs in the EU. This post-approval information demonstrated risks of a different frequency and severity than information previously presented to the FDA.

18. Gilead intentionally withheld a safer alternative design of TDF Drugs it knew to be dangerously toxic to patients' kidneys and bones, while failing to adequately warn about the risks and safer use of the defective drugs, solely to make more money. Accordingly, Plaintiffs bring this action to recover damages for their personal injuries and seek punitive damages arising from Gilead's willful and wanton conduct.

II. JURISDICTION AND VENUE

19. Jurisdiction exists under 28 U.S.C. § 1332(a) because all Plaintiffs and Gilead are citizens of different states and the matter in controversy exceeds the sum or value of $75,000, exclusive of interests and costs.

20. Defendant is subject to in personam in the U.S. District Court for the Middle District of North Carolina because it placed a defective product in the stream of commerce and that product caused personal injuries to Plaintiffs in this District.

21. Venue is proper in this District because reside in this District and a substantial part of the events and omissions giving rise to Plaintiffs' claims occurred in this District.

III. PARTIES

22. Plaintiffs are consumers who ingested one or more of the following TDF Drugs: Viread, Truvada, Atripla, Complera, or Stribild.

23. Plaintiffs suffered personal injuries caused by ingesting TDF.

24. Plaintiff Antonio Gee is and was at all relevant times a citizen of the State of North Carolina and domiciled in Greensboro, North Carolina. Plaintiff Antonio Gee purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Truvada, Atripla and Complera beginning in 2006. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

25. Plaintiff Barry Williams is and was at all relevant times a citizen of the State of North Carolina and domiciled in Fuquay Varina, North Carolina. Plaintiff Barry Williams purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2004. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, and other injuries and damages to be proven at trial.

26. Plaintiff Dewey Goolsby is and was at all relevant times a citizen of the State of North Carolina and domiciled in Hillsborough, North Carolina. Plaintiff Dewey Goolsby purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Viread and Truvada beginning in 2004. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff's ingestion of the TDF Drugs also caused and/or contributed to Plaintiff suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of

these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

27. Plaintiff Donna L. Francis is and was at all relevant times a citizen of the State of North Carolina and domiciled in Winston-Salem, North Carolina. Plaintiff Donna L. Francis purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Atripla beginning in 2006. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

28. Plaintiff Donnie L. Jones is and was at all relevant times a citizen of the State of North Carolina and domiciled in Jacksonville, North Carolina. Plaintiff Donnie L. Jones purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2004. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff

suffering kidney failure and dialysis treatments. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

29. Plaintiff Elizabeth Scoggins is and was at all relevant times a citizen of the State of North Carolina and domiciled in South Mills, North Carolina. Plaintiff Elizabeth Scoggins purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Atripla beginning in 2008. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis and bone fractures. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries, including surgery and physical therapy. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, and has suffered other injuries and damages to be proven at trial.

30. Plaintiff Fernando Samudio is and was at all relevant times a citizen of the State of North Carolina and domiciled in Charlotte, North Carolina. Plaintiff Fernando Samudio purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2006. As a result of Gilead's wrongful conduct with

respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteopenia. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

31. Plaintiff Gaye K. Benton is and was at all relevant times a citizen of the State of North Carolina and domiciled in Chapel Hill, North Carolina. Plaintiff Gaye K. Benton purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Complera beginning in 2011. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries, including physical therapy. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

32. Plaintiff Gerald Fewell is and was at all relevant times a citizen of the State of North Carolina and domiciled in Charlotte, North Carolina. Plaintiff Gerald Fewell purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Viread, Truvada and Atripla beginning in 2001. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering Chronic Kidney Disease and dialysis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

33. Plaintiff Jacqueline Smith is and was at all relevant times a citizen of the State of North Carolina and domiciled in Charlotte, North Carolina. Plaintiff Jacqueline Smith purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Stribild beginning in 2015. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering low kidney functionality. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of

enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

34. Plaintiff James A. Farland is and was at all relevant times a citizen of the State of North Carolina and domiciled in Greensboro, North Carolina. Plaintiff James A. Farland purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2012. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

35. Plaintiff Joseph G. Brisson is and was at all relevant times a citizen of the State of North Carolina and domiciled in Charlotte, North Carolina. Plaintiff Joseph G. Brisson purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Atripla and Truvada beginning in 2006. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a

result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

36. Plaintiff Josephine Porter is and was at all relevant times a citizen of the State of North Carolina and domiciled in Raeford, North Carolina. Plaintiff Josephine Porter purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2004. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of their injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

37. Plaintiff Kimberly S. Jones is and was at all relevant times a citizen of the State of North Carolina and domiciled in Asheboro, North Carolina. Plaintiff Kimberly S. Jones purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2009. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF

Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering acute renal failure. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

38. Plaintiff Lavita Stancil is and was at all relevant times a citizen of the State of North Carolina and domiciled in Durham, North Carolina. Plaintiff Lavita Stancil purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2005. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, and other injuries and damages to be proven at trial.

39. Plaintiff Linda Blackwell is and was at all relevant times a citizen of the State of North Carolina and domiciled in Charlotte, North Carolina. Plaintiff Linda Blackwell purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Truvada and Atripla beginning in 2009. As a result of Gilead's wrongful

conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of bone density loss and a fracture to Plaintiff's foot. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

40. Plaintiff Lynwood Matthews is and was at all relevant times a citizen of the State of North Carolina and domiciled in Rocky Mount, North Carolina. Plaintiff Lynwood Matthews purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2009. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, and other injuries and damages to be proven at trial.

41. Plaintiff Mildred Battiste is and was at all relevant times a citizen of the State of North Carolina and domiciled in Greensboro, North Carolina. Plaintiff Mildred

Battiste purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Atripla beginning in 2008. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

42. Plaintiff Miriam M. Epperson is and was at all relevant times a citizen of the State of North Carolina and domiciled in High Point, North Carolina. Plaintiff Miriam M. Epperson purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2009. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, and has suffered other injuries and damages to be proven at trial.

43. Plaintiff Norman R. Burwell is and was at all relevant times a citizen of the State of North Carolina and domiciled in Durham, North Carolina. Plaintiff Norman R. Burwell purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2006. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, and other injuries and damages to be proven at trial.

44. Plaintiff Pamela V. Gbalah is and was at all relevant times a citizen of the State of North Carolina and domiciled in Chapel Hill, North Carolina. Plaintiff Pamela V. Gbalah purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Truvada, Atripla and Stribild beginning in 2005. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering low kidney function. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost

earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

45. Plaintiff Patricia Walker is and was at all relevant times a citizen of the State of North Carolina and domiciled in High Point, North Carolina. Plaintiff Patricia Walker purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2009. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of weakening of the bones and fractures to Plaintiff's right foot and left heel. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

46. Plaintiff Reggie Eric Briggs is and was at all relevant times a citizen of the State of North Carolina and domiciled in Gastonia, North Carolina. Plaintiff Reggie Eric Briggs purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Atripla beginning in 2009. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis and fractures to Plaintiff's

foot. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, and other injuries and damages to be proven at trial.

47. Plaintiff Regina Taylor is and was at all relevant times a citizen of the State of North Carolina and domiciled in Winston-Salem, North Carolina. Plaintiff Regina Taylor purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Atripla beginning in 2006. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering proteinuria. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, and other injuries and damages to be proven at trial.

48. Plaintiff Robert Timothy Carrington is and was at all relevant times a citizen of the State of North Carolina and domiciled in Raleigh, North Carolina. Plaintiff Robert Timothy Carrington purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Atripla and Truvada beginning in 2006. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused

and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis as well as a fractured finger. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

49. Plaintiff Robert I. Walker is and was at all relevant times a citizen of the State of North Carolina and domiciled in Leicester, North Carolina. Plaintiff Robert I. Walker purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Atripla and Truvada beginning in 2009. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering low kidney function. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

50. Plaintiff Robert Lynn Williamson is and was at all relevant times a citizen of the State of North Carolina and domiciled in Wilmington, North Carolina. Plaintiff

Robert Lynn Williamson purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2017. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

51. Plaintiff Rosemary Wheless is and was at all relevant times a citizen of the State of North Carolina and domiciled in Rocky Mount, North Carolina. Plaintiff Rosemary Wheless purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Truvada and Atripla beginning in 2004. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis and a fracture to Plaintiff's wrist. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental

anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

52. Plaintiff Ruthie Hatcher is and was at all relevant times a citizen of the State of North Carolina and domiciled in Winston-Salem, North Carolina. Plaintiff Ruthie Hatcher purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Atripla beginning in 2006. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, and other injuries and damages to be proven at trial.

53. Plaintiff Shanetta N. Hunter is and was at all relevant times a citizen of the State of North Carolina and domiciled in Raleigh, North Carolina. Plaintiff Shanetta N. Hunter purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Viread, Truvada, and Atripla beginning in 2010. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering kidney failure requiring dialysis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical

treatment as a result of these injuries, including surgery. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

54. Plaintiff Shelia Pinkard is and was at all relevant times a citizen of the State of North Carolina and domiciled in Durham, North Carolina. Plaintiff Shelia Pinkard purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Viread beginning in 2010. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteoporosis. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, and other injuries and damages to be proven at trial.

55. Plaintiff Sonja Livingston is and was at all relevant times a citizen of the State of North Carolina and domiciled in Chapel Hill, North Carolina. Plaintiff Sonja Livingston purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2010. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff

suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

56. Plaintiff Stephen M. Young is and was at all relevant times a citizen of the State of North Carolina and domiciled in Sapphire, North Carolina. Plaintiff Stephen M. Young purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Atripla and Truvada beginning in 2009. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering damage to his kidneys, which resulted in a diagnosis of high creatinine levels. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of their injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

57. Plaintiff Tyrone Brown is and was at all relevant times a citizen of the State of North Carolina and domiciled in Durham, North Carolina. Plaintiff Tyrone Brown purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Atripla beginning in 2006. As a result of Gilead's wrongful conduct with respect to the

defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering bone demineralization, which resulted in a diagnosis of osteopenia. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

58. Plaintiff Vanessa Fulwiley is and was at all relevant times a citizen of the State of North Carolina and domiciled in Charlotte, North Carolina. Plaintiff Vanessa Fulwiley purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Complera and Truvada beginning in 2012. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering renal failure requiring hospitalization. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of her injuries, and other injuries and damages to be proven at trial.

59. Plaintiff Veronica Angela McCullough is and was at all relevant times a citizen of the State of North Carolina and domiciled in Durham, North Carolina. Plaintiff

Veronica Angela McCullough purchased and ingested the following TDF Drug for an FDA-approved use of the drug: Truvada beginning in 2006. As a result of Gilead's wrongful conduct with respect to the defective TDF Drug, Plaintiff ingested and was injured by the foregoing TDF Drug. Plaintiff's ingestion of the TDF Drug caused and/or contributed to Plaintiff suffering acute renal failure. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of their injuries, has suffered lost earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

60. Plaintiff William T. Blue is and was at all relevant times a citizen of the State of North Carolina and domiciled in Lumber Bridge, North Carolina. Plaintiff William T. Blue purchased and ingested the following TDF Drugs for an FDA-approved use of the drugs: Truvada, Atripla and Viread beginning in 2004. As a result of Gilead's wrongful conduct with respect to the defective TDF Drugs, Plaintiff ingested and was injured by the foregoing TDF Drugs. Plaintiff's ingestion of the TDF Drugs caused and/or contributed to Plaintiff suffering Chronic Kidney Disease. Plaintiff required and incurred and will continue to require and incur expenses in connection with medical treatment as a result of these injuries. Plaintiff has endured and will continue to endure pain, suffering, mental anguish, and loss of enjoyment of life as a result of his injuries, has suffered lost

earnings and/or a loss of earning capacity, and other injuries and damages to be proven at trial.

61. Defendant Gilead Sciences, Inc. is a Delaware corporation with its principle place of business at 333 Lakeside Drive, Foster City, California. Gilead is a biopharmaceutical company that develops, manufactures, markets, and sells prescription medicine, including, but not limited to, Viread, Truvada, Atripla, Complera, Stribild, Genvoya, Odefsey, and Descovy. Gilead reported revenue of $26.1 billion dollars in 2017 and has operations worldwide.

IV. FACTUAL ALLEGATIONS

62. Gilead's "Company Overview" states: "With each new discovery and investigational new drug candidate, we seek to improve the care of patients living with life-threatening diseases around the world."[3] It would more accurately state: We seek to improve the care of patients living with life-threatening diseases *only if and when it suits the company's financial needs*.

A. Background

1. Laws and regulations governing the approval and labeling of prescription drugs.

63. The Federal Food, Drug, and Cosmetic Act ("FDCA" or the "Act") requires manufacturers that develop a new drug product to file a New Drug Application ("NDA")

[3] *See, e.g.*, Gilead Sciences Company Overview, available at http://www.gilead.com/~/media/Files/pdfs/other/US%20Corporate%20Overview%20%20111014.pdf.

in order to obtain approval from the Food and Drug Administration ("FDA") before selling the drug in interstate commerce. 21 U.S.C. § 355.

64. The NDA must include, among other things, data regarding the safety and effectiveness of the drug, information on any patents that purportedly cover the drug or a method of using the drug, and the labeling proposed to be used for the drug. 21 U.S.C. § 355(b).

65. Manufacturers with an approved NDA must review all adverse drug experience information obtained by or otherwise received by them from any source, including but not limited to postmarketing experience, reports in the scientific literature, and unpublished scientific papers. 21 C.F.R. § 314.80(b).

66. After FDA approval, manufacturers may only promote drugs in a manner consistent with the contents of the drug's FDA-approved label. 21 C.F.R. § 202.1. The FDA's Division of Drug Marketing, Advertising, and Communications monitors manufacturers' promotional activities and enforces the FDCA and its implementing regulations to ensure compliance.

67. Under what is known as the Changes Being Effected ("CBE") regulation, a manufacturer with an approved NDA can make certain changes to its label without prior FDA approval by simply sending the FDA a "supplemental submission." 21 C.F.R. § 314.70(c)(6)(iii).

68. Changes to the labeling a manufacturer can make pursuant to CBE without prior FDA approval include those to "add or strengthen a contraindication, warning,

precaution, or adverse reactions for which the evidence of causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter" and "to add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." 21 C.F.R. § 314.70(c)(6)(iii)(A) and (C).

69. A manufacturer must revise its label "to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitively established." 21 C.F.R. § 201.57(c)(6).

70. The warnings section of the label "must identify any laboratory tests helpful in following the patient's response or in identifying possible adverse reactions. If appropriate, information must be provided on such factors as the range of normal and abnormal values expected in the particular situation and the recommended frequency with which tests should be performed before, during, and after therapy." Id. § 201.57(c)(6)(iii). According to an FDA Guidance for Industry on the warnings and precautions section of the labeling, "[i]nformation about the frequency of testing and expected ranges of normal and abnormal values should also be provided if available."[4]

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4 https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/
UCM075096.pdf.

71. Adverse reactions must be added to the label where there "is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event." *Id*. § 201.57(c)(7).

72. An August 22, 2008 amendment to these regulations provides that a CBE supplement to amend the labeling for an approved product must reflect "newly acquired information." 73 Fed. Reg. 49609. "Newly acquired information" is not limited to new data but also includes "new analysis of previously submitted data." "[I]f a sponsor submits adverse event information to FDA, and then later conducts a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for 'newly acquired information.'" *Id*. at 49607.

73. Under the 1984 Hatch-Waxman Amendments to the Act, Congress sought to expedite the entry of less expensive generic versions of brand name drugs by simplifying the generic approval process. A generic manufacturer seeking to sell a generic version of a brand name drug may file an Abbreviated New Drug Application ("ANDA"), which relies on the brand manufacturer's safety and efficacy data. The ANDA filer must demonstrate that its proposed generic product is therapeutically equivalent to the brand name drug, meaning that it: (a) contains the same active ingredient(s), dosage form, route of administration, and strength as the brand name drug; and (b) is bioequivalent to the brand drug (i.e., the drugs exhibit the same rate and extent of absorption).

74. As a counter-balance to the abbreviated process for the approval of generic drugs, Hatch-Waxman may grant brand manufacturers a period of market exclusivity upon approval of the NDA. For example, Hatch-Waxman grants a five-year period of exclusivity (regardless of any patent protection) to products containing chemical entities not previously approved by the FDA. Under this five-year exclusivity, the FDA cannot even accept an ANDA to make a generic version of the drug for four or five years from NDA approval (depending upon whether the generic asserted that the brand's patents were invalid or not infringed).

75. Hatch-Waxman also streamlined the process for brand manufacturers to attempt to enforce their patents against potential infringement by generic manufacturers. If an ANDA contains a certification that the patents the brand has listed in its NDA are invalid or will not be infringed by the ANDA generic product (a "Paragraph IV certification"), the brand manufacturer can automatically delay FDA approval of the generic drug by suing the generic manufacturer for patent infringement. If the brand manufacturer brings a patent infringement action against the generic filer within 45 days of receiving notification of the Paragraph IV certification, the FDA may not grant final approval to the ANDA until the earlier of (a) the passage of two and a half years, or (b) the issuance of a court decision that the patent is invalid or not infringed by the generic manufacturer's ANDA. 21 U.S.C. § 355(j)(5)(B)(iii).

76. Generic drugs that are therapeutically equivalent to the brand name drug may be automatically substituted for the brand at the pharmacy counter. Due to state automatic

substitution laws that permit or require generic substitution, once a generic version of a brand-name drug enters the market, the generic quickly captures the vast majority of the brand's sales, often obtaining 80% or more of unit sales within the first six months. On average, generics capture 90% of brand unit sales within the first year of generic entry.

2. Tenofovir and Gilead's TDF- and TAF- containing drug products indicated for use in treating HIV.

77. Tenofovir (chemical name, 9-(2-Phosphonomethoxypropyl)adenine ("PMPA")) is a type of medicine called a nucleotide analog reverse transcriptase and HBV polymerase inhibitor ("NRTI").

78. In order for HIV to infect a healthy human cell, the virus must convert its ribonucleic acid ("RNA") based genome into a strand of complementary deoxyribonucleic acid ("DNA"). This process of converting the virus's RNA into DNA is reverse transcription, and is performed by an enzyme named reverse transcriptase. Reverse transcription occurs inside the human cell that the virus is infecting.

79. NRTIs prevent the reverse transcriptase from converting its RNA into DNA, preventing the infection of the cell and spread of HIV. In order for NRTIs to stop HIV from infecting a cell, the drug must be absorbed into the cell and "activated" by the cell's biological machinery. The "activated" form of tenofovir is known as tenofovir-diphosphate ("TFV-DP").

80. When used to treat HIV infection, tenofovir must be administered in combination with other anti-HIV drugs, a practice known as "combination antiretroviral therapy" or "cART." By using a combination of different classes of medications,

physicians can customize treatment based on factors including how much virus is in the patient's blood, the particular strain of the virus, and disease symptoms. The aim of cART is to reduce the viral load—i.e., the amount of virus per unit of blood or plasma, of patients to levels where commercial viral load tests cannot detect the presence of the virus (generally a concentration of lower than 50 HIV-1 RNA copies per mL of plasma). A cART treatment regimen can incorporate multiple standalone pills or a single pill coformulated with all drugs necessary for the regimen.

81. Gilead did not discover tenofovir. Tenofovir was discovered in the mid-1980s by the collaborative research efforts of scientists in Prague and Belgium. Although the anti-HIV properties of tenofovir were promising, it had a significant downside. When tenofovir is administered by mouth, very little of it is absorbed into the body.

82. Because an intravenous formulation had little sales potential, Gilead developed a prodrug form of tenofovir that can be taken orally. Prodrugs are pharmacologically inactive compounds that can be more efficiently absorbed into the bloodstream and then converted into the active form of the drug within the body.

83. One prodrug of tenofovir is tenofovir disoproxil (chemical name, bis(isopropyloxycarbonyloxymethyl)-PMPA or bis-POC PMPA). The fumaric salt of tenofovir disoproxil is tenofovir disoproxil fumarate, commonly known as TDF.

84. While TDF is able to be taken by mouth, the proportion of tenofovir that enters the cells is relatively low. In order to have the desired therapeutic effect, a high dose of TDF must be administered. The standard dose of TDF for HIV treatment and prevention

in adults is relatively large—300 mg taken once a day. A general principle of toxicology is that the "dose makes the poison"—i.e., larger doses are generally associated with higher rates of toxicity and adverse events. Tenofovir is no different.

85. Gilead has received FDA approval for five TDF-based drugs for the treatment of HIV.

86. On October 26, 2001, the FDA approved Gilead's NDA 21356 for Viread (300 mg TDF) tablets for use in combination with other antiretroviral agents for the treatment of HIV-1 infection. Gilead submitted limited clinical data supporting approval of the drug. Gilead had not completed Phase III clinical studies. Gilead excluded from its clinical trials people who had serious preexisting kidney dysfunction. And Gilead only studied Viread in treatment-experienced patients (those who had previously been treated for HIV). In 2008, the FDA approved an additional Viread indication for the treatment of Chronic Hepatitis B.

87. On August 2, 2004, the FDA approved Gilead's NDA 21752 for Truvada tablets, which is a combination product containing 300 mg TDF (i.e., Viread) and 200 mg emtricitabine, for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults. Neither of the active ingredients in Truvada was new. The FDA approved the Truvada application based primarily on data showing the fixed-dose combination drug was bioequivalent to its separate components. On July 16, 2012, the FDA approved an additional indication for the use of Truvada in combination with safer sex

practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.

88. On July 12, 2006, the FDA approved Gilead's NDA 21937 for Atripla tablets, which is a combination product containing 300 mg TDF, 200 mg emtricitabine, and 600 mg efavirenz, for use alone as a complete regimen or in combination with other retroviral agents for the treatment of HIV-1 infection in adults. Gilead submitted no clinical data in support of NDA 21937. None of the active ingredients in Atripla were new. Approval was based on a demonstration of bioequivalence between the individual components and the fixed-dose combination.

89. On August 10, 2011, the FDA approved Gilead's NDA 202123 for Complera tablets, which is a fixed dose combination product containing 300 mg TDF, 200 mg emtricitabine, and 25 mg rilpivirine, for use as a complete regimen for the treatment of HIV-1 infection in treatment-naïve adults (i.e., adults who had not been previously treated for HIV). None of the active ingredients in Complera were new. Gilead submitted no new clinical safety or efficacy trials in connection with NDA 20123. Approval was based on the results of bioequivalence studies comparing the combination product to the individual component drugs. In addition, the primary focus of the FDA's safety and medical review of the Complera NDA was on rilpivirine, since that drug was the most recently approved component of the fixed dose combination Complera tablet.

90. On August 27, 2012, the FDA approved Gilead's NDA 203100 for Stribild, which is a fixed dose combination product containing 300 mg TDF, 200 mg emtricitabine,

150 mg elvitegravir, and 150 mg cobicistat, for use as a complete regimen for the treatment of HIV-1 infection in treatment-naïve adults. Although elvitegravir and cobicistat had not been previously approved by the FDA, the FDA gave Gilead's Stribild NDA a 10-month standard review because there were already multiple regimens available for treatment naïve patients including one pill, once-a-day regimens.

91. Before the FDA approved Viread in 2001, Gilead had discovered another prodrug version of tenofovir, which it originally called GS-7340 and which is now known as tenofovir alafenamide fumarate ("TAF"). TDF and TAF are two prodrug versions of the same parent drug, tenofovir, though TAF requires a dose more than ten times smaller than TDF to achieve the same therapeutic effect.

92. TAF differs from TDF in its penetration into target cells. Unlike TDF, which is converted into the parent drug tenofovir in the gastrointestinal tract, liver, and blood, TAF is not converted into tenofovir until it has been absorbed by the cell. This allows TAF to be more efficiently absorbed by "target cells"—i.e., cells that HIV infects or "targets"—compared to TDF. This more efficient absorption allows TAF to achieve far greater intracellular concentrations of the activated drug (tenofovir-diphosphate) in target cells than even a dramatically larger dose of TDF. This enhanced efficiency in absorption leads to plasma concentrations of tenofovir that are 90% lower than TDF, while still maintaining intracellular concentrations of activated drug in target cells that is the same or higher than TDF. The lowered plasma concentrations of tenofovir found with TAF result in reduced toxicity compared to TDF, making TAF safer to use than TDF.

93. On November 5, 2015, the FDA approved Gilead's first TAF-based design—NDA 207561 for Genvoya tablets, a fixed dose combination product which contains 10 mg TAF, 200 mg emtricitabine, 150 mg elvitegravir, and 150 mg cobicistat. Genvoya is indicated for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age or older who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least six months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Genvoya. The TDF-based counterpart to Genvoya is Stribild. Genvoya is identical to Stribild except for the substitution of TAF for TDF.

94. On March 1, 2016, the FDA approved Gilead's NDA 208351 for Odefsey tablets, which is a combination product containing 25 mg TAF, 200 mg emtricitabine, and 25 mg rilpivirine, for use as a complete regimen for the treatment of HIV-1 infection in patients 12 years of age and older as initial therapy in those with no antiretroviral treatment history with HIV-1 RNA less than or equal to 100,000 copies per mL; or to replace a stable antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL of blood or plasma) for at least six months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Odefsey. The TDF-based counterpart to Odefsey is Complera. Odefsey is identical to Complera except for the substitution of TAF for TDF.

95. On April 4, 2016, the FDA approved Gilead's NDA 208215 for Descovy tablets, which is a fixed dose combination product containing 25 mg TAF and 200 mg emtricitabine, for use in combination with other antiretroviral agents, for treatment of HIV-1 infection in adults and pediatric patients 12 years of age or older. The TDF-based counterpart to Descovy is Truvada. Descovy is identical to Truvada except for the substitution of TAF for TDF.

96. Upon information and belief, Gilead has not sought FDA approval of a standalone TAF drug product for the treatment of HIV. Viread, therefore, has no TAF-based counterpart for the treatment of HIV infection. Although the FDA approved Gilead's NDA 208464 for Vemlidy (300 mg TAF) tablets on November 10, 2016, Gilead only sought approval to market Vemlidy for the treatment of Hepatitis B infection in adults with compensated liver disease and thus cannot be marketed for the treatment of HIV.

B. Gilead knew before Viread was approved that TDF posed a significant safety risk.

97. Before Gilead's first TDF product, Viread, received FDA approval in 2001, Gilead knew that two of its other antiviral drugs that are structurally similar to tenofovir caused significant kidney damage.

98. Tenofovir is a member of a class of molecules known as "acyclic nucleoside phosphonates." Two of Gilead's other antiviral drugs—cidofovir and adefovir[5]—are also acyclic nucleoside phosphonates.

[5] Like tenofovir, only a prodrug of adefovir—adefovir dipivoxil—can be effectively administered orally.

99. Cidofovir injection, marketed as Vistide, was Gilead's first commercial product. When the FDA approved Vistide in 1996, it carried a black box warning stating that renal impairment is the drug's major toxicity and renal failure resulting in dialysis or contributing to death have occurred with as few as one or two doses of Vistide.

100. In December 1999, Gilead abandoned development of NRTI prodrug adefovir dipovoxil for the treatment of HIV after it proved so toxic to patients' kidneys in the later stages of Phase III clinical trials. In Gilead's clinical trial GS-408, 59% of patients demonstrated severe kidney toxicity after 72 weeks. One patient in the trial died due to multiorgan failure subsequent to kidney failure. Based on this experience, Gilead knew that adefovir dipivoxil was associated with delayed nephrotoxicity—meaning that its toxic effects might not be felt for some time after continued use. Gilead would later develop and market adefovir dipivoxil as Hepsera for treatment of hepatitis B virus infection. Critically, Gilead recognized that if it reduced the dose of adefovir dipivoxil from 120 mg—as used in trial GS-408 for the treatment of HIV—to 10 mg (the dose in Hepsera), an effective dose for hepatitis B virus treatment, the risk of nephrotoxicity is dramatically reduced.

101. Tenofovir has a nearly identical structure to adefovir, varying only by the presence of a methyl group (i.e., a carbon atom bound to three hydrogen atoms) in tenofovir, which replaces a hydrogen atom in adefovir. As Gilead recognized in its 10-K for the year ending December 31, 2000, due to its experiences with nephrotoxicity in Phase III clinical trials of adefovir dipovoxil, delayed toxicity issues similar to those experienced with adefovir dipivoxil could arise with TDF.

102. Gilead also knew that while prodrugs allow the drug to be efficiently absorbed into the bloodstream and then converted into an active form within the body, the conversion of the TDF prodrug into free tenofovir outside the cell, and the presence of high levels of free tenofovir in the blood, endangers the kidneys.

103. The primary purpose of the kidney is to filter out toxins and waste products from the blood, as well as help maintain the delicate balance of water, salts and other compounds in a person's blood. The functional unit of the kidney is the nephron, a microscopic structure that consists of two primary components: a renal "corpuscle" and a renal "tubule." On average, each kidney contains hundreds of thousands to millions of nephrons.

104. The renal corpuscle is the component of the nephron that directly filters the blood. Blood flows through a network of capillaries (small blood vessels) known as the glomerulus. The walls of these capillaries work as a filter, allowing certain compounds, as well as water, to pass through. The fluid that is filtered through the capillary walls in the glomerulus, known as the filtrate, is collected by a structure known as Bowman's capsule. One of the ways kidney function is measured is by the rate of blood that is filtered by the glomeruli. This is known as the glomerular filtration rate or "GFR."[6]

[6] GFR is not measured directly. Physicians typically estimate a patient's GFR by testing for serum creatinine or by calculating creatinine clearance. Creatinine is a waste product that is produced by the breakdown of muscle tissue and created at a relatively constant rate by the body. The kidneys filter creatinine from the blood into the urine, and reabsorb almost none of it. If the kidney is damaged, the ability of the body to remove creatinine from the blood can be reduced, resulting in high levels of creatinine in the blood. Serum creatinine

105. In Bowman's capsule, the filtrate is collected and drains into the other primary component of the nephron, the tubule. Glomerular filtration is highly effective at removing many toxins, but it also filters out many compounds, like water and electrolytes, that a person needs. In the tubule, the cells lining the tubule put these crucial, non-toxic compounds back into the blood, as well as filter out remaining toxins that glomerular filtration did not remove. After the filtrate exits the tubule, it drains into the bladder. This processed filtrate is urine.

106. This system of filtering the blood is extremely important and delicate. TDF primarily damages the nephron tubule, due to hyper-concentration of free tenofovir within the tubule cells of the nephron, which results in cell death or dysfunction. If the tubule cells are dysfunctional or dead, they are unable or less able to perform the vital function of filtering waste and/or toxins and reabsorbing beneficial compounds. Tubular injury can occur without a decline in a patient's glomerular filtration rate. Physicians must monitor other markers of kidney function—those that assess tubule function specifically, like serum phosphorus or urine glucose, to assess a patient's true kidney health.

107. Because tenofovir is renally eliminated, through glomerular filtration and proximal tubular secretion, patients are exposed to an increased concentration of tenofovir as the kidneys become damaged. Because exposure to an increased concentration of

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is the amount of creatinine in the blood. Creatinine clearance is the rate at which the kidneys clear creatinine from the blood and is measured using the amount of creatinine present in urine over 24 hours. As renal function goes down, creatinine clearance also goes down.

tenofovir increases toxicity, patients' kidney function must be monitored to ensure that their kidneys remain healthy enough to receive tenofovir.

108. Since scientists first synthesized TDF, studies have consistently shown that it could cause significant kidney and bone damage. For example, an animal study published in 1999 showed that high doses of tenofovir were associated with significant bone toxicity in both simian immunodeficiency virus (SIV, the non-human primate version of HIV) infected and uninfected rhesus macaques, with a quarter of the treated animals experiencing significant bone toxicity.

109. Gilead's preclinical studies of TDF showed that it could be toxic to kidneys and bones. Preclinical animal studies of TDF showed evidence of renal toxicity and that TDF exposure caused bone toxicity in the form of softening of the bones (osteomalacia) and reduced bone mineral density. Nephrotoxicity in animal models was related to dose as well as to duration of therapy.

110. Gilead also knew that the relatively high dose of TDF needed to achieve the desired therapeutic effect created a greater risk of toxic effects, and that bone and kidney toxicities were even more likely with the long-term use of TDF which was needed to combat a disease with no known cure.

C. Gilead's knowledge of TDF toxicity grew as patients' kidneys and bones were damaged by the TDF Drugs.

111. As soon as Gilead began marketing Viread, patients started experiencing the nephrotoxic effects of TDF.

112. In November 2001, less than one month after Viread entered the market, the first published case of TDF-associated acute renal failure occurred. Thereafter, additional reports of TDF-associated kidney damage, including but not limited to Fanconi syndrome, renal failure, renal tubular dysfunction, and nephrogenic diabetes insipidus, began to appear in the medical literature. Many of those adverse events occurred in patients without preexisting kidney dysfunction.

113. Gilead was also seeing renal adverse events in its postmarketing safety data. In fact, the most common serious adverse events reported to Gilead were renal events, including renal failure,[7] Fanconi syndrome,[8] and serum creatinine increase.

114. In the first two years Viread was on the market, 40% of Viread adverse events reports received by Gilead were related to the renal/urinary system. This included 49 cases of increased creatinine, 16 cases of hypophosphatemia,[9] 42 cases of renal insufficiency, 51 cases of acute renal failure, 6 cases of chronic renal failure, and 32 cases of Fanconi syndrome. These numbers are far less than the true incidence of kidney damage experienced by Viread patients during this timeframe because postmarketing adverse events are underreported.

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[7] When the kidney cannot filter the blood normally, a patient is usually diagnosed with "renal failure."

[8] If damage to the tubule prevents the reabsorption of beneficial molecules from filtrate, the levels of these beneficial compounds can become dangerously low in the blood. This is known as Fanconi syndrome.

[9] Hypophosphatemia is a low level of phosphorus in the blood, which can indicate that the ability of the nephron tubule to reabsorb phosphorus from the filtrate is damaged.

115. Gilead had to update its Viread labeling at least four times to describe the kidney damage patients experienced when taking TDF:

a. On December 2, 2002, Gilead added that patients had suffered renal impairment, including increased creatinine, renal insufficiency, kidney failure, and Fanconi syndrome, with Viread use;

b. On October 14, 2003, Gilead added more kidney disorders, including acute renal failure, proximal tubulopathy,[10] and acute tubular necrosis;[11]

c. On May 12, 2005, Gilead added nephrogenic diabetes insipidus;[12] and

d. On March 8, 2006, Gilead added polyuria[13] and nephritis[14] to the list of renal and urinary disorders that patients had experienced while on TDF.

As Gilead knew, injuries were not limited to patients with a history of renal dysfunction or other risk factors.

116. Gilead's long-term clinical data also demonstrated that TDF was damaging patients' bones. 48-week data showed greater decreases from baseline in bone mineral density at the lumbar spine and hip in patients taking Viread compared to those receiving other HIV drugs. At 144 weeks, there was a significantly greater decrease from baseline in

[10] Proximal tubulopathy refers to damage or dysfunction to the portion of the nephron tubule that is closest to Bowman's capsule.

[11] Acute tubular necrosis refers to the death of the cells that line the nephron tubule. This is associated with loss of kidney function.

[12] Nephrogenic diabetes insipidus refers to a condition characterized by the production of a large amount of dilute urine as a result of kidney dysfunction. It is thought to be related to damage to the nephron tubule.

[13] Polyuria refers to the excessive production of urine.

[14] Nephritis refers to the inflammation of the kidneys.

bone mineral density at the lumbar spine in patients taking Viread compared to those receiving other HIV drugs, as well as significant increases in biochemical markers of bone turnover in patients taking Viread. And once Gilead began conducting clinical trials with Viread in adolescent and pediatric patients, the effects of TDF on adolescent and pediatric patients' bones were similar to the effects seen with adult patients.

117. After Gilead brought Truvada to market, the medical literature continued to identify cases of TDF-associated kidney damage, including in patients without preexisting renal dysfunction or co-administration with another nephrotoxic drug.

118. Several new studies presented at the February 2006 Conference on Retroviruses and Opportunistic Infections ("CROI") highlighted the frequency of nephrotoxicity in TDF-treated patients. In one study, CDC investigators analyzed longitudinal data from 11,362 HIV-infected patients, all of whom had GFR > 90mL/min at baseline, and found that treatment with TDF was significantly associated with mild and moderate renal insufficiency. In another, observational study of 497 patients initiating TDF treatment, 17.5% developed renal dysfunction. The most severe declines in renal function were associated with TDF treatment as part of a boosted regimen.

119. In 2007, Gilead scientists published an article discussing the company's knowledge of TDF safety issues over the first four years of TDF treatment. Gilead reported that 0.5% of patients enrolled in a global expanded access program experienced a serious renal adverse event, including acute and chronic renal failure and Fanconi syndrome. A "serious" adverse event meant one resulting in hospitalization or prolongation of

hospitalization, death, disability, or requiring medical intervention to prevent permanent impairment. Gilead also reported that through April 2005 the most common serious adverse events reported to Gilead's postmarketing safety database were renal events, including renal failure, Fanconi syndrome, and serum creatinine increase.

120. Although this Gilead article demonstrates the company's clear and early knowledge of serious TDF toxicity in a significant number of patients, it downplayed the incidence of TDF-associated renal toxicity. In its Medical Review of the Stribild NDA in 2012, the FDA noted the limitations of Gilead's data, including the short duration of treatment, the voluntary nature of adverse event reporting in some countries, and the fact that Gilead only assessed serious adverse events, and not renal events leading to drug discontinuation or non-serious renal adverse events. According to the FDA, any of these factors may have led to an underestimation of the true incidence of renal events of interest. The FDA similarly questioned Gilead's data on the incidence of renal adverse events based on its postmarketing safety database given the voluntary nature of reporting.

121. Moreover, even if Gilead's data accurately captured the percentage of patients experiencing serious renal adverse events (which it did not), it would still represent a very large number of patients who experienced significant health problems due to TDF toxicity. For example, in late 2015, according to data from Symphony Health Solutions, nearly 500,000 people in the U.S. were ingesting TDF daily. Using Gilead's numbers, approximately 2,500 of those patients would likely experience severe kidney damage. Now

that TDF has been on the market for nearly two decades, many thousands of patients have likely experienced severe TDF-induced kidney damage.

122. In May 2007, Gilead had to update its labeling to recognize that TDF-associated renal damage also caused osteomalacia (softening of the bones) in patients. In November 2008, Gilead modified the labeling to state that patients taking TDF had experienced osteomalacia due to proximal renal tubulopathy as bone pain, and that it might contribute to fractures.

123. In August 2008, Gilead had to update its labeling to recognize finally that TDF caused both "new onset" and "worsening" renal impairment—meaning, as Gilead knew years prior, that TDF was injuring patients' kidneys even though they had no preexisting renal dysfunction.

124. During 2009–2011, studies continued to show that TDF caused a significant loss of renal function in HIV-infected patients.

125. Multiple articles described how the incidence of TDF-induced nephrotoxicity was underreported because studies often excluded patients who were most likely to exhibit nephrotoxic effects, including patients who combined TDF in a ritonavir-boosted regimen or with another nephrotoxic drug, older patients or those with advanced HIV disease, or those with mild baseline renal dysfunction. Notwithstanding selection bias that tended to hide TDF-associated kidney dysfunction, the evidence was clear that TDF caused renal tubular dysfunction in a significant percentage of HIV-infected patients.

126. In April 2012, researchers at the San Francisco Veterans' Administration Medical Center and the University of California, San Francisco published their analysis of the medical records of more than 10,000 HIV-positive veterans in the national VA healthcare system, which is the largest provider of HIV care in the United States. The study authors found that for each year of tenofovir exposure, risk of protein in urine—a marker of kidney damage—rose 34%, risk of rapid decline in kidney function rose 11%, and risk of developing chronic kidney disease rose 33%. The risks remained after the researchers controlled for other kidney disease risk factors such as age, race, diabetes, hypertension, smoking, and HIV-related factors.

127. By the time it reviewed the Stribild NDA, the FDA stated that the safety profile of TDF was, by that point, "well-characterized in multiple previous clinical trials and is notable for TDF-associated renal toxicity related to proximal renal tubule dysfunction and bone toxicity related to loss of bone mineral density and evidence of increased bone turnover."[15]

128. With each passing year and each successive TDF product, Gilead learned even more about TDF's toxicity. Despite this knowledge, Gilead repeatedly designed the TDF Drugs to contain TDF as the tenofovir delivery mechanism rather than safer TAF.

[15] FDA Center for Drug Evaluation and Research Summary Review for NDA 203100 at 10, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203100Orig1s000SumR.pdf.

D. Before Gilead developed Stribild, it knew that renal adverse events were more likely when patients took TDF as part of a boosted regimen.

129. Before Gilead first started marketing Viread, it knew that patients' exposure to tenofovir increases significantly when tenofovir is co-administered with a ritonavir-boosted protease inhibitor: the maximum concentration of tenofovir increased 31%; the minimum concentration of tenofovir increased 29%; and the area under the curve (the actual body exposure to the drug after dose administration) increased 34%.

130. In the first few years TDF was on the market, many reported cases of tenofovir-related renal damage involved patients taking TDF with a ritonavir-boosted protease inhibitor—leading authors to conclude that the risk of TDF-associated renal toxicity increased for patients on a boosted regimen. This is consistent with other patient populations at increased risk for renal toxicity, including those with low body weight and those taking another nephrotoxic drug; each is associated with higher levels of tenofovir exposure.

131. As Gilead recognized in the Precautions section of the July 1, 2004 Viread label: "[h]igher tenofovir concentrations could potentiate Viread-associated adverse events, including renal disorders."[16]

132. Gilead further stated: "Atazanavir [another protease inhibitor] and lopinavir/ritonavir have been shown to increase tenofovir concentrations. The mechanism of this interaction is unknown. Patients receiving atazanavir and lopinavir/ritonavir and

[16] Viread (tenofovir disoproxil fumarate) Tablets label at 17, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2004/21356slr010_viread_lbl.pdf.

Viread should be closely monitored for Viread-associated adverse events. Viread should be discontinued in patients who develop Viread-associated adverse events."[17]

133. Case study authors similarly called for careful monitoring of patients taking TDF in a boosted regimen, given the frequency of renal damage in such patients.

134. A 2008 Journal of Infectious Diseases article reported that the odds of developing significant renal function reduction were 3.7 times higher for patients receiving a regimen containing tenofovir plus ritonavir-boosted protease inhibitor than for those receiving tenofovir plus nonnucleoside reverse transcriptase inhibitor-based therapy, even after adjusting for viral load.

E. Before Gilead developed each of the TDF Drugs, it knew that TAF was less toxic to kidneys and bones than TDF.

135. Before the FDA approved Viread, Gilead had already discovered a different design for an orally available version of tenofovir that is more potent than TDF, meaning that it can be administered at a significantly lower dose with fewer side effects than TDF.

136. Unlike TDF, TAF is not converted into tenofovir until it has been absorbed by the cell. As a result, TAF is more efficiently absorbed by the cells HIV targets compared to TDF. This more efficient absorption allows TAF to achieve far greater intracellular concentrations of the activated drug (tenofovir-diphosphate) in target cells than even a dramatically larger dose of TDF, while achieving plasma concentrations of tenofovir that

[17] *Id.*

are 90% lower than TDF. The lowered plasma concentrations of tenofovir found with TAF result in reduced toxicity compared to TDF, making TAF safer to use than TDF.

137. On July 21, 2000, Gilead filed a provisional patent application which described TAF (then called GS-7340) as 2–3 times more potent than TDF while providing 10 times the intracellular concentration of tenofovir than TDF. Gilead also demonstrated that dosing with TAF resulted in dramatically higher concentrations of drug in all organs except the kidneys and the liver, compared with TDF. This suggested that TAF is uniquely able to target cells that HIV infects, while not concentrating in the kidney.

138. In a 2001 paper, Gilead scientists described the remarkable results achieved when studying the metabolism of TAF in blood. The paper, "Metabolism of GS-7430, A Novel Phenyl Monophosphoramidate Intracellular Prodrug of PMPA, In Blood," compared the distribution of the active drug tenofovir in blood cells and plasma after exposure to either GS-7430 or tenofovir disoproxil (which was still in clinical development at the time of the study). What Gilead found was that one need only ***one thousandth of the dose*** of GS-7340 compared to tenofovir to achieve the same level of inhibition of HIV replication in vitro. Gilead also found that one need to use only one tenth the dose of GS-7340 compared to TDF to reach the same levels of active tenofovir inside cells.

139. Gilead researchers presented the results of its GS-7340 study at a February 2002 Conference on Retroviruses. John Milligan, then Gilead's Vice President of Corporate Development and currently its President and Chief Executive Officer, said that Gilead's goal with GS-7340 was to deliver a more potent version of tenofovir that can be

taken in lower doses, resulting in better antiviral activity and fewer side effects. Milligan said that "there's a great need to improve therapy for HIV patients."[18]

140. Gilead's preclinical studies of TAF also indicated that TAF is less likely to accumulate in renal proximal tubules than TDF, supporting the potential for an improved renal safety profile.

141. Gilead's 2001 10-K highlighted the benefits of GS-7340 over Viread: "Both GS 7340 and Viread are processed in the body to yield the same active chemical, tenofovir, within cells. However, the chemical composition of GS 7340 may allow it to cross cell membranes more easily than Viread, so that with GS 7340, tenofovir may be present at much higher levels within cells. As a result, GS 7340 may have greater potency than Viread and may inhibit low-level HIV replication in cells that are otherwise difficult to reach with reverse transcriptase inhibitors."[19]

142. At the end of the first quarter of 2002, Gilead told investors that it had initiated Phase I/II testing of GS-7340. In an earnings call, Gilead stated that it had initiated a dose escalation study for GS-7340 through which Gilead intended to prove that GS-7340 was more potent than Viread, meaning that it could be administered at a safer, lower dose.

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[18] Special Coverage: 9th Conference on Retroviruses – New drugs, new data hold promise for next decade of HIV treatment, AIDS Alert, May 1, 2002.

[19] Gilead Sciences, Inc. Form 10-K for the fiscal year ended December 31, 2001, at 13, available at https://www.sec.gov/Archives/edgar/data/882095/000091205702011690/a2073842z10-k.htm.

143. In an October 28, 2003 earnings call, Gilead told analysts that data from the ongoing Phase I/II study of GS-7340 "look[ed] promising."[20]

144. In December 2003, Mark Perry, then Gilead's Executive Vice President of Operations, told investors that Gilead was "excited" about GS-7340. Gilead expected GS-7340 to achieve "more potency at lower doses and increase the therapeutic index for" tenofovir.[21] The "therapeutic index" is a comparison of the amount of a therapeutic agent that causes the therapeutic effect compared to the amount that causes toxicity.

145. In January 2004, Gilead repeatedly referred to the positive results from clinical studies of GS-7340 in calls with analysts and disclosures to the investment industry. On a January 29, 2004 earnings call, Gilead stated that, based on these positive results, it was designing a Phase II program for GS-7340 to determine the safety and efficacy of the compound in treatment naïve patients and in highly treatment experienced patients.

146. At a May 2004 Deutsche Bank Securities Healthcare Conference, Gilead said that it knew GS-7340 could be dosed at a fraction of the Viread dose and give a greater antiviral response.

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[20] Event Brief of Q3 2003 Gilead Sciences Earnings Conference Call – Final, FD (Fair Disclosure) Wire, Oct. 28, 2003.

[21] Gilead Sciences at Harris Nesbitt Gerard Healthcare Conference 2003 – Final, FD (Fair Disclosure) Wire, Dec. 11, 2003.

147. However, on October 21, 2004, shortly after the FDA approved Truvada, Gilead abruptly announced that it would abandon its GS-7340 design. It stated:

> Earlier this year as a result of positive data from a small phase I/II study of GS 7340, we began designing a phase II program to determine the safety and efficacy of the compound in treatment-naive patients and in highly treatment experienced patients. Since that time we have witnessed the increasing use of Viread across all HIV patient populations, and we have also received approval for and launched Truvada.
>
> Based on our internal business review and ongoing review of the scientific data for GS 7340, we came to the conclusion that it would be unlikely that GS 7340 would emerge as a product that could be highly differentiated from Viread.[22]

148. Prior to its October 2004 announcement, Gilead never indicated that there might be an issue with differentiating GS-7340 from Viread or expressed any other negative view of the prospects of GS-7340. To the contrary, Gilead repeatedly touted the positive results of preclinical and clinical studies of GS-7340 and the benefits of GS-7340 over Viread.

149. Gilead's "internal business review" was the real driver of its decision to abandon a design it knew to be safer than Viread.

150. In May 2005, despite Gilead's misrepresentation that GS-7340 was not worth pursuing, Gilead scientists reported the favorable results they achieved with GS-7340,

[22] https://www.gilead.com/news/press-releases/2004/10/gilead-discontinues-development-of-gs-9005-and-gs-7340-company-continues-commitment-to-research-efforts-in-hiv.

including its benefits over Viread, in an issue of Antimicrobial Agents and Chemotherapy. Reuters Health News covered the article:

> After oral administration of GS 7340 to dogs, tenofovir concentrations were 5- to 15-fold higher in lymph nodes than after tenofovir DF administration, the researchers note. Except for kidney and liver, tissue concentrations of tenofovir were generally higher after GS 7340 than after tenofovir DF administration.
>
> "The high concentrations of tenofovir observed in lymphatic tissues after oral administration of GS 7340 are expected to result in increased clinical potency relative to tenofovir DF and could have a profound effect on the low-level virus replication that occurs in tissues with suboptimal drug exposure during HAART," the authors conclude.
>
> "With GS 7340," the researchers add, "it should be possible to reduce the total dose of tenofovir, thereby minimizing systemic exposure, while at the same time increasing antiviral activity."[23]

151. Moreover, even though Gilead purportedly abandoned TAF, Gilead filed seven applications for patents on TAF between 2004 and 2005.

152. Despite recognizing the safety benefits of TAF, Gilead kept its GS-7340 design on the shelf for years—knowingly exposing patients taking its TDF-containing drug products to greater risks of kidney and bone toxicity.

153. It was not until approximately October 2010—***six years*** after Gilead shelved its safer tenofovir prodrug and after Gilead designed combination products Truvada and Atripla to contain TDF rather than safer TAF—that Gilead renewed development of the safer TAF design.

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[23] Novel tenofovir prodrug preferentially targets lymphatic tissue, Reuters Health Medical News, June 1, 2005.

154. Once Gilead renewed development of its TAF design, it again touted the benefits of TAF over TDF—as if it had never falsely claimed that TAF could not be "highly differentiated" from TDF.

155. Despite having discovered the benefits of TAF before 2001, Gilead repeatedly misrepresented TAF as "new." The benefits of TAF that Gilead described in 2010 and beyond were known to Gilead years earlier. And the clinical results Gilead achieved with TAF would have been achieved years earlier but for Gilead's decision to slow-walk and withhold the safer TAF design purely for financial gain.

156. In an October 19, 2010 earnings call, Gilead's Chief Scientific Officer Norbert Bischofberger explained to investors how GS-7340's safety profile was superior to Viread, particularly with respect to kidney and bone toxicity:

> 7340 is a prodrug that actually delivers more active antivirally active components into the compartment in the body where it's really needed which means lymphocytes mostly. What that means is you can take a lower dose, and actually our clinical study would indicate 1/6th to 1/10th the Viread dose and you would actually get higher efficacy with less exposure. So we're looking at this to be used in sub population where people have a concern with Viread, and the one with renal impairment, elderly people that have reduced renal function, and the other population will be adults that have preexisting or suspicion of bone disease, osteoporosis, and that's where we are initially going to position the compound.[24]

157. Giving a statement at the Capital Markets Healthcare Conference on March 2, 2011, John Milligan, then Gilead's President and Chief Operating Officer, told investors

[24] Q3 2010 Gilead Sciences Earnings Conference Call – Final, FD (Fair Disclosure) Wire, Oct. 19, 2010.

the real reason Gilead previously refused to design its products to contain safer GS-7340—it did not want to hurt TDF sales by stepping on its TDF marketing message:

> One of the reasons why we were concerned about developing 7340 was we were trying to launch Truvada versus Epzicom[25] at that time. And to have our own study suggesting that Viread wasn't the safest thing on the market, which it certainly was at the time. … It didn't seem like the best. It seemed like we would have a mix[ed] message. And in fact that Viread story is split out to be a fairly safe product over the years. There are some concerns still on kidney toxicity and there are some concerns about bone toxicity.[26]

158. Milligan called GS-7340 a "kinder, gentler version of Viread."[27]

159. At the March 14, 2011 Roth Capital Partners Growth Stock Conference, Gilead stated that the ability to dose GS-7340—the "kinder, gentler" version of Viread—lower than Viread was important because GS-7340 is safer, particularly as patients take the medication for the long term.[28]

160. At the NASDAQ OMS 26th Investor Program in June 2011, Gilead described GS-7340 as a "very exciting product" which was then in dosing studies to determine just how low GS-7340 could be dosed. Gilead explained the benefit of lower dosing to aging patients and those who have been on the medication for a long time:

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[25] Epzicom is a combination medication, containing abacavir and lamivudine, indicated to treat HIV sold by Gilead's competitor GlaxoSmithKline, now Viiv Healthcare, Ltd. The FDA approved both Epzicom and Truvada in August 2004.

[26] Gilead Sciences at RBC Capital Markets Healthcare Conference – Final, FD (Fair Disclosure) Wire, Mar. 2, 2011.

[27] *Id*.

[28] Gilead Sciences at Roth Capital Partners OC Growth Stock Conference – Final, FD (Fair Disclosure) Wire, Mar. 14, 2011.

> And we had recently this year had presented 14-day monotherapy results from a study we had done at 50 and 100 mg of 7340 versus the 300 mg of Viread today. And what we have shown was viral load reductions were greater in the lower doses of 7340 and the plasma tenofovir levels were actually much reduced from what we see with Viread.
>
> We're currently now in a Phase Ib looking at even lower doses. We are studying 8 mg, 25 and 40 mg of GS-7340. This is important because as the age of the AIDS population continues to increase, as the median age is now just about 50 years old, you get issues with aging such as renal function and bone mineral density that can become bigger issues for these patients and we think that it's a currently unmet medical need to address those concerns of the aging population in HIV.[29]

Yet, Gilead knew well before 2010–2011 that people with HIV were living longer lives. Since the introduction of effective combination antiretroviral therapy in late 1995 and early 1996, many people with HIV have lived a normal lifespan.

161. On January 24, 2012, Gilead announced that it had begun Phase II clinical trials of GS-7340 and identified a dose that is ten times lower than Viread while providing greater antiviral efficacy.

162. On October 31, 2012, Gilead announced that a Phase II clinical trial evaluating TAF met its primary objective. The study compared a once-daily single tablet regimen containing TAF 10 mg/elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg with Stribild (TDF 300 mg/elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg) among treatment-naïve adults. Compared to Stribild, the TAF-containing regimen demonstrated better markers of bone and kidney effects that were statistically significant.

[29] Gilead Sciences Inc. at NASDAQ OMS 26th Investor Program – Final, FD (Fair Disclosure) Wire, June 21, 2011.

The study showed that TAF is effective at a fraction of the dose of Viread and provides safety advantages.

163. In January 2013, Gilead began Phase III clinical development of TAF. Announcing the beginning of Phase III development, then-CEO Martin mischaracterized TAF as "new."[30]

164. Gilead finally submitted an application to market its first TAF-containing product, Genvoya, to the FDA on November 5, 2014 (though it could have done so years earlier had it not shelved the safer design to make more money).

165. When the FDA approved Genvoya on November 5, 2015, John C. Martin, then Chairman and CEO of Gilead, announced that "there is still a need for new treatment options that may help improve the health of people as they grow older with the disease."[31] Martin misrepresented that TAF was "new" and concealed that Gilead had known about this safer version of tenofovir for over a decade but purposefully withheld it from the market solely to protect its monopoly profits and extend Gilead's ability to profit on TAF regimens for the next decade or more.

[30] Gilead Sciences at JPMorgan Global Healthcare Conference – Final, FD (Fair Disclosure) Wire, Jan. 7, 2013.

[31] US FDA approvals Gilead's Single Table Regiment Genvoya for Treatment of HIV-1 Infection, Business Wire, Nov. 5, 2015.

F. Gilead withheld its safer TAF design to protect its TDF sales and extend profits on its HIV franchise.

166. Gilead first developed and sought FDA approval for its TDF line of products even though it knew TAF was safer.

167. Then Gilead shelved its TAF design in 2004 because it did not want to hurt TDF sales by admitting that TDF is unreasonably and unnecessarily unsafe.

168. Gilead continued to withhold its TAF design for the next decade. Gilead knew that by withholding the safer TAF design, it could extend the longevity of its HIV drug franchise and make billions two times over: first, with TDF medications until TDF patent expiration, which would begin by no later than 2018, and second, with TAF medications until TAF patent expiration as late as 2032.

169. But Gilead also knew that timing was key. While it wanted to delay the TAF-designed products to maximize profits on its TDF Drugs, it also knew that it had to get its TAF-based products on the market sufficiently in advance of TDF patent expiration. Gilead knew that once doctors switched their patients from TDF to TAF, doctors would be highly unlikely to switch their patients back to TDF-based regimens once generic TDF became available. By converting TDF prescriptions to TAF prescriptions (which cannot be automatically substituted at the pharmacy counter with a generic TDF product), Gilead could save a substantial percentage of sales from going generic.

170. Only once Gilead had realized billions in sales through most of the TDF patent life—having built Viread sales up to $1.1 billion and the TDF portfolio up to $11

billion in sales in 2015—did Gilead create TAF-based versions of its prior TDF Drugs and work to convert its TDF Drug sales to TAF drug sales.

171. Once TAF entered the market, Gilead successfully convinced a large percentage of doctors to switch from TDF-based to TAF-based regimens by highlighting TAF's improved safety profile with respect to bone and kidney toxicity—the very benefits that Gilead could have and should have incorporated into its product design from the beginning but withheld from patients with each successive TDF Drug for over a decade.

172. In addition, by delaying the filing of an NDA for its first TAF product, for which it received five-year regulatory exclusivity, Gilead knew that it was also delaying the entry of any generic manufacturer who could successfully challenge Gilead's TAF patents as invalid or not infringed. Due to its regulatory exclusivity, no generic manufacturer can even file an ANDA with a Paragraph IV certification seeking to market a generic version of Genvoya until November 2019 and then, upon Gilead's suit against the generic, Gilead can automatically delay generic entry by up to an additional 30 months.

173. Gilead boasted about TAF's potential to extend its HIV franchise, which has been the core of its business.

174. Milligan told investment analysts in 2010 that the safer TAF-designed products could replace the whole TDF franchise which would provide a "great deal of longevity. …"[32] Milligan similarly told investors at a Deutsche Bank Securities Inc.

[32] Gilead Sciences at 22nd Annual Piper Jaffray Healthcare Conference – Final, FD (Fair Disclosure) Wire, Nov. 30, 2010.

Healthcare Conference in May 2011 that TAF was a "new" drug that "could potentially bring quite a bit of longevity to the Gilead portfolio."[33]

175. As Milligan told analysts at a Goldman Sachs Global Healthcare Conference in June 2011, Gilead would be "offering a product called 7340, which we believe is a lower dose, better safety profile, more potent, differentiated drug relative to Viread. And so, our ability to develop and get that onto the market prior to [TDF] patent expiration will be key to us, to maintain the longevity."[34]

176. Gilead withheld its safer TAF design until it suited Gilead's bottom line at the expense of patients' health.

G. Gilead knowingly designed its TDF drugs to be unreasonably dangerous and unsafe to patients' kidneys and bones.

177. Despite knowing that TDF causes kidney and bone damage and that TAF is safer for patients' kidneys and bones, Gilead designed the TDF Drugs to contain TDF rather than safer TAF as the orally available version of tenofovir.

178. In addition to withholding the safer TAF design of Stribild, Gilead made Stribild even more dangerous to patients when it formulated the drug to include 300 mg TDF with cobicistat.

[33] Gilead Sciences Inc. at Deutsche Bank Securities Inc. Health Care Conference – Final, FD (Fair Disclosure) Wire, May 3, 2011.

[34] Gilead Sciences Inc. at Goldman Sachs Global Healthcare Conference – Final, FD (Fair Disclosure) Wire, June 7, 2011.

179. Stribild is a fixed dose combination containing 300 mg TDF, emtricitabine, elvitegravir, and cobicistat. Elvitegravir is an integrase strand transfer inhibitor (INSTI). Cobicistat has no antiretroviral effect; it is a pharmacoenhancer that increases the plasma concentrations of elvitegravir. Regimens that include a pharmacoenhancer like cobicistat are called "boosted" regimens.

180. Gilead's early development of elvitegravir used ritonavir as the boosting agent. Gilead knew before Viread entered the market in 2001 that coadministration of TDF with ritonavir-boosted lopinavir significantly increased tenofovir concentrations. By 2004, the Viread label warned doctors to carefully monitor patients taking both TDF and ritonavir/lopinavir. And scientific literature published years before Gilead developed Stribild indicated that renal toxicity associated with TDF was more frequent in patients receiving TDF in combination with boosted protease inhibitors.

181. Although Gilead ultimately replaced ritonavir with cobicistat as the boosting agent in Stribild, the two boosters are structurally similar. Gilead learned during development of Stribild that tenofovir levels in patients receiving Stribild (TDF with cobicistat) were similar to the tenofovir levels experienced in patients who took TDF in combination with a ritonavir-boosted protease inhibitor. Gilead knew that tenofovir levels are 25–35% higher when combining TDF in a boosted regimen.

182. Despite knowing that combining TDF with cobicistat would significantly increase tenofovir levels in patients' blood, Gilead did not reduce the dose of TDF when it formulated Stribild. Gilead's Stribild clinical trials showed an increased rate of serious

renal adverse events that led to treatment discontinuation. Stribild is even more toxic to patients' kidneys and bones than unboosted TDF.

183. When Gilead formulated its first TAF-based drug, Genvoya—which was Stribild with TAF in place of TDF—Gilead reduced the dose of TAF to account for the fact that cobicistat increases tenofovir concentrations. A Phase I TAF dosing trial showed that TAF 25 mg was the optimal dose to achieve activity similar to a 300 mg dose of TDF. When formulating Genvoya, however, Gilead further reduced the TAF dose to 10 mg because, when given with cobicistat, TAF 10 mg achieves exposure similar to TAF 25 mg when given without cobicistat.

184. Gilead knew to reduce the dose of TAF to 10 mg when given with cobicistat before Gilead sought FDA approval for Stribild. Pursuant to Gilead's Phase I study GS-US-311-0101, conducted between June 6, 2011 and August 31, 2011, Gilead determined that co-administration of TAF with cobicistat significantly increased the body's exposure to TAF and active tenofovir. It found that the body's drug exposure across time (known as the "area under the curve" in pharmacokinetic parlance) increased 2.7-fold with respect to TAF and 3.3-fold with respect to tenofovir when given with cobicistat. Gilead addressed this drug interaction by reducing the dose of TAF from 25 mg to 10 mg in the Genvoya tablet. When Gilead began its study GS-US-292-0103 on October 5, 2011, it used a TAF dose of 10 mg in the Genvoya combination because "the TAF dose is 10 mg when

combined with COBI in the [fixed dose combination] versus 25 mg when not combined with COBI."[35]

185. Critically, Gilead reduced the TAF dose when formulating Genvoya even though patients' plasma exposure to tenofovir when taking TAF is already significantly less than their tenofovir exposure when taking TDF due to TAF's enhanced entry and absorption into target cells.

186. Moreover, in July 2011, months before Gilead submitted its Stribild NDA to the FDA, Gilead sought FDA approval of reduced doses of TDF (Viread) in 150 mg, 200 mg, and 250 mg strengths for the treatment of HIV-1 infection in pediatric patients ages 2-12. That same month, Gilead also sought approval of Viread 40 mg oral powder for the treatment of HIV-1 infection in pediatric patients 2 years and older.[36] The FDA approved the lower dosage strength TDF tablets and oral powder in early January 2012—over six months before the FDA approved the Stribild NDA. There was no reason Gilead could not have similarly reduced the dose of TDF in Stribild—when it knew that failing to reduce the dose would increase the drug's toxicity.

187. As a direct result of Gilead's decision not to use a safer design, Stribild proved to be toxic to patients' kidneys and bones.

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[35] FDA Center for Drug Evaluation and Research, Genvoya NDA 207561 Clinical Pharmacology and Biopharmaceutics Review(s) at 32, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/207561Orig1s000ClinPharmR.pdf.

[36] In the EU, Gilead recommends that adults with creatinine clearance below 50 mL/min take Viread oral powder to reduce their doses of TDF.

188. In the clinical trials of Stribild over 48 weeks, eight patients in the Stribild group compared to one in the comparator groups discontinued the drug study due to renal adverse events, including kidney failure and Fanconi Syndrome. Four of these patients developed laboratory findings consistent with proximal renal tubular dysfunction. The laboratory findings in these four subjects improved but did not completely resolve upon discontinuation of Stribild. The signature toxicity of the Stribild group was proximal renal tubular dysfunction.

189. The FDA's Medical Review described the notable adverse events that led to study discontinuation more frequently in the Stribild group as a "constellation of renal [Adverse Events] (e.g. renal failure, Fanconi syndrome, and increased blood creatinine)."[37]

190. According to the FDA, the "most important safety risks of Stribild use are associated with two key toxicities: renal adverse events (particularly proximal renal tubular dysfunction) and bone toxicity. Both of these events have previously been associated with use of TDF …."[38]

191. The FDA noted that "published literature suggests that the renal toxicity associated with TDF may be more frequent in patients receiving TDF in combination with

[37] FDA Center for Drug Evaluation and Research Stribild NDA 203100 Medical Review at 9, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203100Orig1s000MedR.pdf.

[38] FDA Center for Drug Evaluation and Research Stribild NDA 203100 Cross Discipline Team Member Review at 17, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203100Orig1s000CrossR.pdf.

PIs, including ritonavir,"[39] and the "review team remains concerned that COBI may exacerbate the known renal toxicity associated with TDF."[40] In its Summary Review of the Stribild NDA, the FDA concluded: "it appears that the combination of COBI with TDF may have more renal toxicity than TDF alone as highlighted in the clinical reviews and the renal consult."[41] The FDA expressed concern that the data reviewed for the Stribild NDA represented an increased hazard signal even compared to regimens containing TDF combined with another boosting agent.

192. Due to Stribild's renal toxicity, Stribild use is restricted in patients with impaired renal function. Stribild's label states that doctors should not initiate Stribild in patients with estimated creatinine clearance below 70 mL per minute, and Stribild should be discontinued if estimated creatinine clearance declines below 50 mL per minute as dose interval adjustment cannot be achieved. Moreover, in the EU—though not in the U.S. — Gilead warns doctors that Stribild should not be initiated in patients with creatinine clearance below 90 mL per minute unless, after review of all available treatment options, it is considered that Stribild is the preferred treatment for the individual patient.

193. Gilead's post-approval Stribild data continued to show renal adverse effects. In the clinical trials of Stribild over 96 weeks, two additional Stribild patients discontinued

[39] *Id*. at 18.

[40] *Id*.

[41] FDA Center for Drug Evaluation and Research Stribild NDA 203100 Summary Review at 16, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203100Orig1s000SumR.pdf.

the study due to a renal adverse reaction. In the clinical trials of Stribild over 144 weeks, three additional Stribild patients discontinued the study due to a renal adverse reaction. In addition, one patient who received ritonavir-boosted atazanavir plus Truvada (i.e., a boosted TDF regimen) in the comparator group developed laboratory findings consistent with proximal renal tubular dysfunction leading to drug discontinuation after week 96.

H. Gilead obtained FDA approval for its TAF-based products by relying on studies demonstrating TAF's superiority over TDF.

194. In seeking FDA approval of its first TAF-based antiviral drug product, Genvoya, Gilead told the FDA that TAF has better entry and concentration in HIV-target cells than TDF, thereby allowing the administration of smaller doses and reducing systemic tenofovir exposure, renal toxicity and bone effects, without sacrificing efficacy.

195. Gilead established during Phase I clinical development of TAF that doses as low as 8 to 25 mg of TAF had antiviral activity comparable to the approved dose of TDF 300 mg. Gilead selected the 25 mg TAF dose as the optimal dose for Phase 2 and 3 studies based on its antiviral activity. Gilead included TAF 10 mg in Genvoya because it provides similar exposures to TAF 25 mg when coadministered with cobicistat.

196. Gilead supported the safety and efficacy of Genvoya with two clinical trials that compared Genvoya to its TDF-containing counterpart, Stribild. In those studies, a 10 mg oral dose of TAF in Genvoya resulted in greater than 90% lower concentrations of active tenofovir in plasma as compared to a 300 mg oral dose of TDF in Stribild. Due to these lower plasma concentrations, Gilead expected that the kidney and bone toxicities associated with TDF would occur at a lower rate with TAF. And, as expected, the trials

showed that rates of biomarkers for tenofovir-induced renal and bone toxicities were less with Genvoya than Stribild.

197. In seeking FDA approval of Genvoya in 2014, Gilead relied on TAF data obtained by Gilead more than a decade earlier—before the company abruptly shelved its TAF design in pursuit of more money. Gilead submitted in its Genvoya NDA data from: (a) early clinical development showing that TAF provided greater intracellular distribution of tenofovir yielding lower plasma tenofovir levels than TDF; (b) preclinical studies that indicated TAF is less likely to accumulate in renal proximal tubules, supporting the potential for an improved renal safety profile; and (c) Phase I dosing studies supporting doses of TAF far lower than the standard 300 mg dose of TDF.

198. Reviewing these studies, the FDA stated that: "Based on the design of the pivotal clinical trials, safety can be directly compared between TAF (Genvoya) and TDF (as Stribild) in subjects initiating treatment."[42] According to the FDA, the studies showed that "the rates of signature TFV [tenofovir] toxicities related to bone mineral density and renal laboratory parameters were lower [than TDF], likely due to the fact that the TAF prodrug yields lower plasma concentrations of TFV."[43]

199. As a result of its improved renal safety profile over TDF, Gilead's TAF-containing products are better tolerated by patients with renal impairment.

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[42] FDA Center for Drug Evaluation and Research Genvoya NDA 207561 Summary Review at 10, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/207561Orig1s000SumR.pdf.

[43] *Id*. at 15.

200. For example, Genvoya requires no dosage adjustment for patients with creatinine clearance greater than or equal to 30 mL per minute, whereas its TDF-containing counterpart Stribild is not recommended for patients with creatinine clearance below 70 mL per minute and Stribild should be discontinued if creatinine clearance falls below 50 mL per minute as dose interval adjustment cannot be achieved. Due to its superior safety profile, Genvoya has an expanded indication for renally impaired individuals with creatinine clearance greater than or equal to 30 mL per minute.

201. As a result of its improved bone toxicity safety profile over TDF, the labels for Gilead's TAF-containing products no longer include bone effects in the Warnings and Precautions sections of those labels.

202. The FDA agreed that bone effects need only be displayed in the Adverse Events section of TAF drug labeling because "[w]ith respect to bone toxicity, TAF appears to have substantially less of an adverse effect on bone mineral density (BMD) than TDF."[44]

203. Gilead removed bone toxicity from the Warnings and Precautions sections of the Genvoya label in December 2016 and from the Odefsey and Descovy labels in 2017. Bone toxicity remains in the Warnings and Precautions sections of the labels of Gilead's TDF Drugs to this day.

[44] FDA Center for Drug Evaluation and Research Vemlidy NDA 208464 Summary Review at 5, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/208464Orig1s000SumR.pdf.

I. Gilead markets TAF as superior to TDF.

204. Gilead's TAF-based product websites, including the Genvoya site, market the TAF-based drugs as superior to Gilead's TDF-containing products with respect to kidney health. Gilead recognizes that: "Kidneys play a key role in keeping you healthy, working around the clock to remove waste from your blood. That's why it's so important to take care of them, especially if you have HIV-1."[45] Gilead states that the TAF-based products have "less impact on kidney lab tests" than other approved HIV-1 treatments, including Stribild, Atripla, and Truvada. The website also highlights that unlike its TDF products, the TAF-based products are "FDA-approved for people with mild-to-moderate kidney problems and can be used in some people with lowered kidney function without changing the dose."[46]

205. Gilead's TAF-based product websites, including the Genvoya site, market the TAF-based drugs as superior to Gilead's TDF-containing products with respect to bone health. Gilead recognizes that: "Because HIV-1 medicines may impact your bones, it's important to protect your bone health. If you're under 30 years of age, you're still developing bone mass. If you're over 30, your bones have fully developed and it's important to try to maintain them."[47] The site touts clinical studies which demonstrate that

[45] *See* https://www.genvoya.com/hiv-kidney-bone-health.

[46] *Id*.

[47] *Id*.

the TAF-containing products "had less impact on hip and lower spine bone mineral density than the other approved HIV-1 treatments," including Stribild, Atripla, and Truvada.[48]

206. Gilead also touts TAF as safer than TDF to scientists, clinical investigators, and doctors attending the annual Conference on Retroviruses and Opportunistic Infections ("CROI").

207. In 2015, Gilead scientists presented to CROI attendees data evaluating the safety and efficacy of Genvoya in patients with mild to moderate renal impairment. Gilead stated that "TDF has been associated with clinically significant renal and bone toxicity," and "[r]elative to TDF 300 mg, TAF at an equivalent dose of 25 mg has 90% lower circulating plasma TFV, while maintaining high antiviral activity."[49] This first study of a single-tablet antiviral regimen without dose adjustment in patients with mild to moderate renal impairment demonstrated the efficacy and renal and bone safety of Genvoya in this patient population.

208. In 2016, Gilead scientists presented to CROI attendees data evaluating the renal safety of TAF in patients with a high risk of kidney disease. Gilead stated that TDF "has been associated with an increased risk of [chronic kidney disease] …." and "[d]ue to a 91% lower plasma tenofovir level, tenofovir alafenamide (TAF) relative to TDF has demonstrated a significantly better renal safety profile and no discontinuations due to renal adverse events through 2 years in 2 randomized, double-blind studies … comparing TAF

[48] *Id*.

[49] http://www.croiconference.org/sites/default/files/posters-2015/795.pdf.

to TDF ….”[50] With respect to high risk renal patients, Gilead concluded that “[a]ntiretroviral-naïve adults with both high and low risk for [chronic kidney disease] treated with TAF had more favorable renal outcomes compared to those treated with TDF.”[51]

209. Gilead also presented at the 2016 CROI data demonstrating that TAF is safer to kidneys than TDF in the longer-term. Showing data through 96 weeks, Gilead concluded that “[c]linically significant renal events were less frequent in patients receiving” TAF vs. TDF and these “data provide further support for the improved renal safety profile of TAF compared with TDF.”[52]

210. In 2017, Gilead scientists presented to CROI attendees data showing that switching patients with low bone mineral density from a TDF-based to a TAF-based regimen results in increased BMD and a reversion from osteoporosis, leading Gilead to conclude that “[s]witching from TDF to TAF may be an important treatment strategy to increase bone mineral density in those at the highest fracture risk.”[53]

211. Also in 2017, Gilead scientists presented to CROI attendees 144-week data establishing the superiority of TAF over TDF with respect to efficacy as well as kidney and bone safety. At week 144, TAF: was “superior to [TDF] on virologic efficacy,” had

[50] http://www.croiconference.org/sites/default/files/posters-2016/681.pdf.
[51] *Id*.
[52] http://www.croiconference.org/sites/default/files/posters-2016/682.pdf.
[53] http://www.croiconference.org/sites/default/files/posters-2017/683_Brown.pdf.

"significantly less impact than [TDF] on renal biomarkers," and had "significantly less impact than [TDF] on BMD."[54]

212. In 2018, Gilead scientists presented to CROI attendees 96-week data that showed that switching to a TAF-based regimen resulted in "significant increases in bone mineral density at hip and spine" and "improved biomarkers of renal tubular function."[55]

213. Gilead's sales force has used data showing the superior safety profile of TAF over TDF to convince doctors to switch patients from TDF-based to TAF-based products.

214. Gilead President and COO Milligan told analysts during a November 10, 2015 Credit Suisse Healthcare Conference that he expected Gilead's sales representatives to be successful in switching the market from TDF to Genvoya based on favorable data showing the benefits of TAF over TDF. Milligan viewed switching patients from Stribild to Genvoya as "the most likely thing to happen very commonly, because it's very seamless for the patient. You're not really changing much; you're just getting a better version of Stribild."[56] Milligan also touted the benefit of switching Atripla patients, who, at that point, had a decade of TDF toxicity buildup, to Genvoya, which, he said, gives patients the benefits of TDF with a better safety profile.

215. In order to prevent or combat the cumulative buildup of kidney and bone toxicity associated with TDF (which Gilead itself caused by withholding the safer TAF

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[54] http://www.croiconference.org/sites/default/files/posters-2017/453_Arribas.pdf.

[55] http://www.croiconference.org/sites/default/files/posters-2018/1430_Mills_504.pdf.

[56] Gilead Sciences Inc. at Credit Suisse Healthcare Conference – Final, FD (Fair Disclosure) Wire, Nov. 10, 2015.

design), Gilead's message was: "if you're a new patient, start with a TAF-based single-tablet regimen, because that's going to be highly efficacious and very safe and very tolerable for long-term usage. And if you're on a Viread-based regimen, it's a great idea to convert, switch, upgrade to a TAF-based regimen as soon as possible."[57]

216. According to Milligan, Genvoya was the most successful launch ever for an HIV therapy. After six months on the market, Genvoya was the most prescribed regimen for treatment-naïve and switch patients.

217. Gilead's conversion strategy continued with FDA approval of Gilead's subsequent TAF-based products. As Milligan stated in March 2016, the marketplace was moving to TAF because patients need the safest possible medication:

> [A]s I look at TAF right now there's a very strong medical rationale for TAF versus Viread. And so what we're seeing in the marketplace with the launch of Genvoya and then with the recent approval of Odefsey is the desire to move patients from a TDF containing regimen to a TAF containing regimen … it's very interesting that the field wants to move to the safest medication, I think should move to the safest medication because it's a great opportunity for patients to stay on care for another 10 to 20 years which is really where we're at with most of these patients. They're going to need decades more care and so you need the gentlest, safest option for patients….[58]

[57] Gilead Sciences Inc. at Piper Jaffray Healthcare Conference – Final, FD (Fair Disclosure) Wire, Dec. 1, 2015.

[58] Gilead Sciences Inc. at Barclays Global Healthcare Conference – Final, FD (Fair Disclosure_ Wire, Mar. 15, 2016.

218. Gilead's 2017 Annual Report attributes strong growth in its HIV business to "widespread physician acceptance and uptake" of the TAF-based regimens.[59]

219. In January 2018, Milligan stated that "physicians and patients prefer TAF dramatically over our TDF-containing backbones," noting that its TAF-based products had achieved more than 56% of the market share of its TDF-containing regimen.[60] TAF-based products now make up at least 74% of Gilead's TDF- and TAF-based drug products for HIV treatment.

220. Gilead could have and should have incorporated the benefits of TAF, which doctors and patients "prefer dramatically" over TDF, into its products years earlier.

221. Gilead funded a 2018 study, Baumgardner, J., *et al.*, "Modeling the impacts of restrictive formularies on patients with HIV," that highlights the damage Gilead did by withholding TAF products from the market. The authors found that a restrictive drug formulary design,[61] which restricts access to TAF or TDF-sparing regimens (other antiviral drugs, abacavir, lamivudine, and dolutegravir), forcing more people to use TDF-containing regimens, would cause 171,500 more cumulative bone and renal events and 16,500 more deaths by 2025 compared to an open formulary design which permitted patients to start on TAF. Gilead itself prevented patients from taking TAF for more than a decade—longer

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[59] Gilead Sciences 2017 Year in Review at 7, available at https://www.gilead.com/-/media/files/pdfs/yir-2017-pdfs/final-year-in-review-426.pdf?la=en&hash=E86C6471302682C56A548CC42342AFC4.

[60] Gilead Sciences Inc. at JPMorgan Healthcare Conference – Final, FD (Fair Disclosure) Wire, Jan. 8, 2018.

[61] A drug formulary is a list of an insurer's covered drugs and is designed to save money.

than the period covered by the 2018 study. Gilead likely caused even more deaths and injuries as a result of its callous decision to withhold the safer TAF drugs.

J. Gilead failed to adequately warn about the risks of TDF.

222. In addition to withholding a safer TAF-based design despite knowing the risk its TDF Drugs posed to patients' kidneys and bones, Gilead failed to adequately warn physicians and patients about the risks and safe use of TDF.

1. Gilead failed to adequately warn doctors about the risks of TDF.

223. Because tenofovir is primarily cleared out of the body by the kidneys, a patient experiences even greater exposure to tenofovir as the kidneys become impaired—causing even greater harm. As a result, early detection is key to preventing serious, potentially irreversible renal injury. Frequent monitoring for TDF-induced toxicity is also critical because patients are typically asymptomatic in the early stages. Gilead, however, downplayed the risks of TDF and the need to carefully monitor all patients in order to inflate sales.

224. During the first years Viread was on the market, Gilead relied on Viread sales for a significant portion of its operating income. For 2002, Viread's first full year on the market, Viread sales comprised 53% of Gilead's total product sales. In 2003, Viread accounted for 68% of Gilead's total product sales.

225. Gilead stated in its 2002 10-K that its operations would suffer if Viread did not maintain or increase its market acceptance. Gilead also stated that if additional safety issues were reported for Viread, this could "significantly reduce or limit our sales and

adversely affect our results of operations."[62] Gilead made similar statements in its 2003 and 2004 10-K filings.

226. To make sure that safety issues did not depress or slow the growth of Viread sales, which were crucial to Gilead's operations, Gilead dramatically increased its sales force and marketing budget, and trained its sales representatives to deceptively represent Viread's safety profile. At the direction of Gilead's senior management, Gilead representatives told doctors that Viread was a "miracle drug," "extremely safe," and "extremely well-tolerated" with "no toxicities." Gilead's sales representatives did not tell doctors the facts: that Viread posed significant risks to patients' kidneys and bones.

227. According to a 2009 shareholder lawsuit filed against Viread, Viread's then-Chief Executive Officer John C. Martin frequently referred to Viread as a "miracle drug" at sales force meetings. According to a former employee, Gilead was trying to overcome the perception in the medical community that Viread was like Gilead's previous HIV drugs and would likely cause kidney damage.

228. On March 14, 2002, FDA sent Gilead a Warning Letter admonishing Gilead for engaging in promotional activities that contained false and misleading statements in violation of the Federal Food, Drug and Cosmetic Act. The FDA stated that Gilead

[62] Gilead Sciences, Inc. Form 10-K for the fiscal year ended Dec. 31, 2002 at 24 available at https://www.sec.gov/Archives/edgar/data/882095/000104746903008695/a2105292z10-k.htm.

unlawfully minimized Viread's risks, including with respect to kidney toxicity, and overstated its efficacy.

229. Despite this warning, Gilead continued to unlawfully promote Viread by minimizing its safety risks. During a June 2003 sales force training, Gilead instructed sales representatives to respond to anticipated physician concerns about Viread's nephrotoxicity by downplaying that many patients taking Viread had experienced the adverse effects of kidney toxicity—some of them severe —including but not limited to renal failure, acute renal failure, Fanconi syndrome, proximal tubulopathy, increased creatinine, and acute tubular necrosis. Gilead's sales representatives omitted this material information from their sales presentations in order to drive sales.

230. The FDA issued another Warning Letter to Viread on July 29, 2003, stating that Gilead's sales representatives had repeatedly omitted or minimized material facts regarding the safety profile of Viread. Among other things, the FDA required Gilead to retrain its sales force to ensure that Gilead's promotional activities complied with the Federal Food, Drug and Cosmetic Act and accompanying regulations. But Gilead had achieved its goal: rapidly increased Viread sales.

231. In subsequent years, Gilead continued to downplay the risks of TDF-induced toxicity when promoting its TDF Drugs to doctors by withholding information about the frequency and severity of adverse kidney and bone events; dismissing case reports of acute renal failure and other TDF-associated adverse events as purportedly unavoidable side

effects of tenofovir in an otherwise "safe" drug; and failing to tell doctors to monitor patients for drug-induced toxicity using more sensitive markers of kidney function.

232. In addition to omitting crucial facts about the safety profile of TDF when promoting TDF to doctors, Gilead also downplayed the importance of patient monitoring in its TDF Drug labeling despite the importance of early detection of TDF-induced toxicity. The dangerous inadequacies in Gilead's drug labeling were compounded by the misleading marketing messages it gave to doctors.

233. From Viread's product approval on October 26, 2001, through May 20, 2007, Gilead's TDF labeling failed to warn doctors that all patients needed to be monitored for adverse kidney effects. During this time, Gilead only recommended monitoring patients taking TDF Drugs for renal adverse effects if patients were at risk for, or had a history of, renal impairment or if they were taking another nephrotoxic drug. This monitoring recommendation was woefully inadequate because, as Gilead was well aware, TDF-associated renal toxicity had harmed patients who were not at risk for, or did not have a history of, renal impairment.

234. Gilead failed to include any warning about the need to monitor bone effects until October 14, 2003, and that warning was limited to patients with certain risk factors. Since then, Gilead has only suggested that doctors monitor, and only informs patients that monitoring may be necessary, for patients with certain risk factors for bone adverse effects. Gilead's inadequate kidney monitoring warnings also prevented doctors from detecting early signs of kidney damage that can lead to bone density loss.

235. Gilead failed to warn about the need for universal monitoring even though it knew that all patients taking TDF are at risk for renal and bone adverse effects.

236. Gilead failed to warn about the need for universal monitoring even after patients without preexisting risk factors experienced kidney and bone effects.

237. Gilead failed to warn about the need for universal renal monitoring even though patients with a certain level of renal impairment should not take its TDF products or, if TDF products are to be administered to certain renally impaired patients, the dosing interval must be adjusted. The Viread and Truvada labels require a dosing interval adjustment for patients with creatinine clearance of 30–49 mL per minute, and Atripla and Complera cannot be taken by patients with a creatinine clearance of less than 50 mL per minute. Frequent monitoring of all patients' kidney function is necessary to ensure that patients' kidneys are healthy enough to continue treatment or patients receive a needed dose interval adjustment.

238. Presented with signs of nephrotoxicity, physicians could have weighed further treatment options, such as increased monitoring, less frequent dosing, or drug discontinuation, before the damage manifested, worsened, or became irreversible. By failing to warn doctors to monitor all patients for TDF-associated toxicity, Gilead delayed the diagnosis of TDF-associated harm, causing or enhancing injuries that would have been prevented or lessened through early detection.

239. On May 21, 2007, Gilead added to the Viread label a recommendation that doctors calculate creatinine clearance (one measure of kidney function) in all patients

before initiating treatment with a TDF-based product and as clinically appropriate during therapy. Gilead recommended monitoring of creatinine clearance and serum phosphorus only for patients at risk for renal impairment.[63]

240. The "all patients" monitoring recommendation for Viread, Truvada, Atripla, and Complera remained inadequate because it instructed doctors to assess just one, insufficiently sensitive marker of kidney function.[64] Without using sufficiently sensitive markers of kidney function, substantial kidney injury can occur before it is measurable. As a result, the detection of TDF-induced nephrotoxicity often comes too late, resulting in kidney injury that may be irreversible. Gilead should have warned doctors to test all patients for additional markers of kidney function, such as serum phosphorus and/or urine glucose, which are more sensitive to changes in the nephron tubule, the main site of TDF damage.[65]

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[63] Gilead did not add similar warnings to the Truvada and Atripla labels until 2008. Complera's label included such a warning at the time of FDA approval in 2011. And when Gilead began marketing Stribild in 2012, it warned doctors to assess some measures of kidney function in all patients but failed to warn doctors to monitor all patients for serum phosphorus. These warnings remained inadequate.

[64] It was not until 2018 that Gilead strengthened the Truvada, Atripla, and Complera labels to recommend that all patients receive monitoring for serum creatinine, estimated creatinine clearance, urine glucose, and urine protein. Gilead did not make this change to the Viread label until December 2018, after Plaintiffs filed suit.

[65] The "all patients" monitoring recommendation for Stribild upon approval was inadequate because it failed to warn doctors to measure serum phosphorus. On August 30, 2017, Gilead strengthened the Stribild label to recommend that all patients be monitored for serum creatinine, serum phosphorus, estimated creatinine clearance, urine glucose, and urine protein. But, on August 8, 2018, Gilead again weakened the Stribild label to warn doctors to monitor serum phosphorus only in patients with chronic kidney disease.

241. Phosphorus is a mineral that plays an important role in many physiologic systems, including keeping bones healthy and strong. Normal working kidneys maintain balanced levels of phosphorus in the blood. Low levels of phosphorus in the blood may be indicative of impaired kidney function. Moreover, low serum phosphate is itself dangerous; low levels of phosphorus in the blood can cause a range of health problems, including serious bone and heart damage.

242. Serum phosphorus is a more sensitive marker of nephron tubule function than creatinine clearance. The nephron tubule is responsible for reabsorbing phosphorus from the glomerular filtrate. When the nephron tubule is damaged, it cannot reabsorb enough phosphorus, allowing the phosphorus to be excreted via urine. TDF nephrotoxicity is generally characterized by tubular dysfunction that precedes a decline in glomerular filtration. Thus, by monitoring patients' serum phosphorus, doctors are able to pick up more subtle changes in kidney function that would otherwise go undetected. Moreover, TDF-induced bone injuries are related to the wasting of minerals through the urine. This is due to dysfunction in the nephron tubule, which prevents reabsorption of minerals from the glomerular filtrate. If physicians knew earlier that their patients' kidneys were dysfunctional, subsequent bone injuries could be avoided.

243. Presented with early signs of nephrotoxicity, physicians could have weighed further treatment options, such as increased monitoring or drug discontinuation, before the damage manifested, worsened, or became irreversible. By failing to warn doctors to monitor additional, more sensitive markers of all patients' kidney function, Gilead delayed

the diagnosis of TDF-associated harm, causing or enhancing patients' injuries that would have been prevented or lessened through early detection.

244. Gilead's "all patients" monitoring recommendation for its TDF Drugs also remains inadequate because it fails to instruct doctors how frequently doctors should assess patients' kidney function. By the time a doctor assesses a patient's kidney function when "clinically appropriate," the patient is likely to have already experienced adverse toxic effects, some of which might be irreversible. Regularly scheduled, frequent monitoring of kidney function is necessary to catch early signs of TDF-induced toxicity and prevent injury because patients are generally asymptomatic during the early stages.

245. Moreover, after May 21, 2007, the TDF labels do not disclose that adverse kidney and bone events occurred in patients without preexisting risk factors—which, combined with the warning to only routinely monitor patients at risk—gives the false impression that TDF is only harmful to people otherwise at risk for kidney and bone injuries. By failing to warn doctors as to the frequency of monitoring, Gilead delayed the diagnosis of TDF-associated harm, causing or enhancing injuries that could have been prevented or lessened through early detection.

246. Gilead's monitoring instructions for at risk patients taking Viread, Truvada, Atripla, and Complera, and patients taking Stribild are also inadequate because they fail to recommend a specific, frequent monitoring schedule for doctors to assess patients' kidney function.

247. Gilead's warnings about the need to monitor patients for the renal effects of TDF in the U.S. are far weaker than those given by Gilead to physicians and patients in the European Union. From the approval of the first TDF product in the EU, Gilead's European labeling (known there as the Summary of Product Characteristics or "SmPC") has recommended that doctors in the EU routinely monitor, on a specific schedule, all patients taking TDF Drugs for adverse renal effects. In addition, Gilead's "all patient" monitoring instruction in the EU is not limited to testing only for creatinine clearance. In its EU labeling, Gilead recommends that doctors also monitor all TDF Drug patients' serum phosphorus levels on the specified, frequent schedule.

248. Gilead's renal monitoring instructions for Viread upon approval in the U.S. and the EU looked like this—with Gilead warning EU physicians to monitor all patients' serum creatinine and serum phosphate at baseline and every four weeks, while it told U.S. doctors to consider monitoring only patients at risk, with no recommended frequency:

Viread U.S. Label 10/26/01	**Viread EU Label 02/07/2002**
Although tenofovir-associated renal toxicity has not be observed in pooled clinical studies for up to one year, long term renal effects are unknown. **Consideration should be given to monitoring for changes in serum creatinine and serum phosphorus in patients at risk or with a history of renal dysfunction**.	Although no significant nephrotoxicity has been observed in clinical trials … the monitoring of renal function is recommended since nephrotoxicity of tenofovir cannot be strictly excluded. **The monitoring of renal function (serum creatinine and serum phosphate) is recommended at baseline before taking tenofovir disoproxil fumarate and at routine intervals during therapy every four weeks**.

249. Gilead's EU label also instructed physicians when to increase monitoring and consider treatment interruption in light of the results of frequent monitoring. Gilead's U.S. label contained no such warning:

Viread U.S. Label 10/26/01	Viread EU Label 02/07/2002
	If serum phosphate is < 1.5 mg/dl (0.48 mmol/l) or serum creatinine is > 1.7 mg/dl (150 µmol/l), renal function should be re-evaluated within one week. Consideration should be given to interrupting treatment with tenofovir disoproxil fumarate in patients with increases in serum creatinine to > 2.0 mg/dl (177 µmol/l) or decreases in serum phosphate to < 1.0 mg/dl (0.32 mmol/l).

250. On December 8, 2004, Gilead updated Viread's EU labeling to change the recommended renal monitoring schedule and recommend that doctors monitor creatinine clearance, which gives a more accurate picture of kidney function, rather than serum creatinine.[66] Gilead continued to instruct doctors in the EU to monitor TDF patients more carefully than it instructed doctors in the U.S.:

Viread's U.S. Labeling 12/8/2004	Viread's EU Labeling 12/8/2004
Patients at risk for, or with a history of, renal dysfunction and patients receiving concomitant nephrotoxic agents **should be carefully monitored for changes in serum creatinine and phosphorus.**	**Monitoring of renal function (creatinine clearance and serum phosphate) is recommended before taking tenofovir disoproxil fumarate, every four weeks during the first year, and then every three months. In patients at risk** for, or with a history of, renal dysfunction, and patients with renal insufficiency,

[66] Gilead did not recommend that doctors monitor creatinine clearance in the U.S. until 2007.

Viread's U.S. Labeling 12/8/2004	Viread's EU Labeling 12/8/2004
	consideration should be given to more frequent monitoring of renal function.

251. Like the initial EU label, the 2004 EU label also instructed physicians when to increase monitoring and consider treatment interruption in light of the results of frequent monitoring. Although Gilead instructed U.S. doctors to adjust the dose interval for patients with creatinine clearance <50 mL/min, it did not tell doctors to monitor for creatinine clearance (only serum creatinine for some patients) and only instructed doctors to monitor patients' serum creatinine if they were at risk for, or had a history of, renal impairment:

Viread's U.S. Labeling 12/8/2004	Viread's EU Labeling 12/8/2004
Dosing interval adjustment is recommended in all patients with creatinine clearance <50 mL/min.	If serum phosphate is < 1.5 mg/dl (0.48 mmol/l) or creatinine clearance is decreased to < 50 ml/min, renal function should be re-evaluated within one week and the dose interval of Viread adjusted (see 4.2). Consideration should also be given to interrupting treatment with tenofovir disoproxil fumarate in patients with creatinine clearance decreased to < 50 ml/min or decreases in serum phosphate to < 1.0 mg/dl (0.32 mmol/l).

252. After Gilead began recommending in its U.S. labeling that doctors calculate creatinine clearance in all patients prior to initiating therapy and as clinically appropriate during therapy, Gilead still gave stronger warnings in the EU—recommending that EU doctors monitor all patients' creatinine clearance and serum phosphate every four weeks during the first year, then every three months:

Viread's U.S. Labeling 05/21/2007	Viread's EU Labeling 05/21/2007
It is recommended that creatinine clearance be calculated in all patients prior to initiating therapy and as clinically appropriate during therapy with VIREAD. **Routine monitoring of calculated creatinine clearance and serum phosphorus should be performed in patients at risk for renal impairment.**	It is recommended that creatinine clearance is calculated in all patients prior to initiating therapy with tenofovir disoproxil fumarate and **renal function (creatinine clearance and serum phosphate) is also monitored every four weeks during the first year, and then every three months. In patients at risk** for renal impairment, **consideration should be given to more frequent monitoring of renal function.**

253. Gilead instructs in Viread's most recent EU labeling "that renal function (creatinine clearance and serum phosphate) [should be] assessed in all patients prior to initiating therapy with tenofovir disoproxil fumarate and … also monitored after two to four weeks of treatment, after three months of treatment, and every three to six months thereafter in patients without renal risk factors." For patients at risk for renal impairment, Gilead states that more frequent monitoring of renal function is "required."

254. Gilead has updated its Viread EU labeling multiple times every year since 2002. Each time, Gilead determined that it should instruct doctors in the EU that they should monitor all patients' kidneys on a frequent, specific schedule using multiple markers of kidney function, including serum phosphorus.

255. On February 24, 2005, Truvada received approval to be marketed in the EU. As with Viread, Gilead's Truvada EU labeling contained stronger monitoring warnings than its U.S. labeling at the time of approval:

Truvada's U.S. Labeling 08/02/2004	Truvada's EU Labeling 02/24/2005
Patients at risk for, or with a history of, renal dysfunction and patients receiving	**Careful monitoring of renal function (serum creatinine and serum phosphate)**

Truvada's U.S. Labeling 08/02/2004	Truvada's EU Labeling 02/24/2005
concomitant nephrotoxic agents **should be carefully monitored for changes in serum creatinine and phosphorus**.	**is recommended before taking Truvada, every four weeks during the first year, and then every three months**. In patients with a history of renal dysfunction or **in patients who are at risk for renal dysfunction, consideration should be given to more frequent monitoring of renal function.**

256. Like its Viread EU labeling, Gilead's Truvada EU labeling also instructed physicians to increase monitoring and consider treatment interruption if the results of frequent monitoring showed that a patient's serum phosphate or creatinine clearance fell below a specified level. Gilead's U.S. labeling recommended only that patients with creatinine clearance < 50 mL/min receive a dose adjustment—though Gilead did not recommend that doctors monitor patients' creatinine clearance (and would not do so for almost three years) and only instructed doctors to monitor patients' serum creatinine if they were at risk for, or had a history of, renal impairment.

257. In Truvada's most recent SmPC, Gilead continues to instruct doctors as to frequent, routine monitoring of renal function (creatinine clearance and serum phosphate) for patients without preexisting risk factors for renal disease: at treatment initiation and then "after two to four weeks of use, after three months of use and every three to six months thereafter." For patients at risk for renal disease, Gilead warns that more frequent monitoring of renal function is "required."

258. Gilead has updated its Truvada EU labeling multiple times every year since 2005. Each time, Gilead determined that it should instruct doctors in the EU to monitor all

patients' kidneys on a frequent, specific schedule using multiple markers of kidney function, including serum phosphorus.

259. In 2006, Gilead issued a "Dear Doctor" letter to physicians in the EU about the importance of frequent, routine monitoring of all TDF patients' renal function. Gilead issued no such letter to doctors in the U.S., though the risk to patients' kidneys was the same.

260. On December 18, 2007, Atripla received approval to be marketed in the EU. As with Viread and Truvada, Gilead's Atripla EU labeling contained stronger monitoring warnings than its U.S. labeling at the time of approval:

Atripla's U.S. Labeling 07/12/2006	**Atripla's EU Labeling 12/18/2007**
Patients at risk for, or with a history of, renal dysfunction and patients receiving concomitant nephrotoxic agents **should be carefully monitored for changes in serum creatinine and phosphorus**.	**It is recommended that creatinine clearance is calculated in all patients prior to initiating therapy with Atripla and renal function (creatinine clearance and serum phosphate) is also monitored every four weeks during the first year and then every three months**. In patients with a history of renal dysfunction or in **patients who are at risk** for renal dysfunction, **consideration must be given to more frequent monitoring of renal function.**

261. Like its Viread EU and Truvada EU labeling, Gilead's Atripla EU labeling also instructed physicians to increase monitoring and consider treatment interruption if the results of frequent monitoring showed that a patient's serum phosphate or creatinine clearance fell below a specified level. Gilead's U.S. labeling stated only that patients with

creatinine clearance < 50 mL/min should not receive Atripla—though Gilead did not recommend that doctors monitor patients' creatinine clearance (and would not do so for approximately another year) and only instructed doctors to monitor patients' serum creatinine if they were at risk for, or had a history of, renal impairment:

Atripla's U.S. Labeling 07/12/2006	**Atripla's EU Labeling 12/18/2007**
Since ATRIPLA is a combination product and the dose of the individual components cannot be altered, patients with creatinine clearance <50 mL/min should not receive ATRIPLA.	If serum phosphate is < 1.5 mg/dl (0.48 mmol/l) or creatinine clearance is decreased to < 50 ml/min in any patient receiving Atripla, renal function must be re-evaluated within one week, including measurements of blood glucose, blood potassium and urine glucose concentrations (see section 4.8, proximal tubulopathy). Since Atripla is a combination product and the dosing interval of the individual components cannot be altered, treatment with Atripla must be interrupted in patients with confirmed creatinine clearance < 50 ml/min or decreases in serum phosphate to < 1.0 mg/dl (0.32 mmol/l).

262. In Atripla's most recent SmPC, Gilead instructs doctors that creatinine clearance should be calculated in all patients prior to initiating therapy and renal function (creatinine clearance and serum phosphate) be monitored after two to four weeks of use, after three months of treatment and every three to six months thereafter in patients without renal risk factors. For patients at risk, Gilead states that more frequent monitoring is "required."

263. Gilead has updated its Atripla EU labeling multiple times every year since 2007. Each time, Gilead determined that it should instruct doctors in the EU to monitor all

patients' kidneys on a frequent, specific schedule using multiple markers of kidney function, including serum phosphorus.

264. On November 30, 2011, Complera (under the trade name Eviplera) received approval to be marketed in the EU. As with Viread, Truvada, and Atripla, Gilead's Complera EU labeling contained stronger monitoring warnings than its U.S. labeling at the time of approval:

Complera's U.S. Labeling 08/10/2011	Complera's EU Labeling 11/30/11
It is recommended that creatinine clearance be calculated in all patients prior to initiating therapy and as clinically appropriate during therapy with COMPLERA. **Routine monitoring of calculated creatinine clearance and serum phosphorus should be performed in patients at risk** for renal impairment, including patients who have previously experienced renal events while receiving HEPSERA.	It is recommended that creatinine clearance is calculated in all patients prior to initiating therapy with Eviplera and **renal function (creatinine clearance and serum phosphate) is also monitored every four weeks during the first year and then every three months. In patients at risk** for renal impairment, including patients who have previously experienced renal events while receiving adefovir dipivoxil, **consideration should be given to more frequent monitoring of renal function**.

265. Like its Viread EU, Truvada EU, and Atripla EU labeling, Gilead's Complera EU labeling also instructed physicians to increase monitoring and consider treatment interruption if the results of frequent monitoring showed that a patient's serum phosphate or creatinine clearance fell below a specified level. Gilead's U.S. labeling stated only that patients with creatinine clearance < 50 mL/min should not receive Complera:

Complera's U.S. Labeling 08/10/2011	Complera's EU Labeling 11/30/11
Since COMPLERA is a combination product and the dose of the individual	If serum phosphate is < 1.5 mg/dl (0.48 mmol/l) or creatinine clearance is

Complera's U.S. Labeling 08/10/2011	Complera's EU Labeling 11/30/11
components cannot be altered, patients with creatinine clearance below 50 mL per minute should not receive COMPLERA.	decreased to < 50 ml/min in any patient receiving Eviplera, renal function should be re-evaluated within one week, including measurements of blood glucose, blood potassium and urine glucose concentrations (see section 4.8, proximal tubulopathy). Since Eviplera is a combination product and the dosing interval of the individual components cannot be altered, treatment with Eviplera must be interrupted in patients with confirmed creatinine clearance decreased to < 50 ml/min or decreases in serum phosphate to < 1.0 mg/dl (0.32 mmol/l).

266. In Complera's/Eviplera's most recent SmPC, Gilead instructs that creatinine clearance should be calculated in all patients prior to initiating therapy and renal function (creatinine clearance and serum phosphate) be monitored after two to four weeks of use, after three months of treatment and every three to six months thereafter in patients without renal risk factors. For patients at risk, Gilead states that more frequent monitoring is "required."

267. Gilead has updated its Complera EU labeling multiple times every year since 2011. Each time, Gilead determined that it should instruct doctors in the EU to monitor all patients' kidneys on a frequent, specific schedule using multiple markers of kidney function, including serum phosphorus.

268. On May 27, 2013, Stribild received approval to be marketed in the EU. As with Viread, Truvada, Atripla, and Complera, Gilead included in its Stribild EU labeling stronger monitoring warnings than its U.S. labeling at the time of approval:

Stribild U.S. Labeling 08/27/2012	Stribild's EU Labeling 05/27/2013
Estimated creatinine clearance, urine glucose and urine protein should be documented in all patients prior to initiating therapy…. **Routine monitoring of estimated creatinine clearance, urine glucose, and urine protein should be performed during STRIBILD therapy in all patients. Additionally, serum phosphorus should be measured in patients at risk for renal impairment**.	Creatinine clearance should be calculated and urine glucose and urine protein should be determined in all patients … **Creatinine clearance, serum phosphate, urine glucose and urine protein should be monitored every four weeks during the first year and then every three months during Stribild therapy**. **In patients at risk** for renal impairment **consideration should be given to more frequent monitoring of renal function**.

269. Gilead also included in its Stribild EU labeling a stronger warning about initiating the drug in patients with mild renal impairment:

Stribild U.S. Labeling 08/27/2012	Stribild's EU Labeling 05/27/2013
STRIBILD should not be initiated in patients with estimated creatinine clearance below 70 mL per min.	Stribild should not be initiated in patients with creatinine clearance < 70 mL/min. **It is recommended that Stribild is not initiated in patients with creatinine clearance < 90 mL/min unless, after review of the available treatment options, it is considered that Stribild is the preferred treatment for the individual patient**.

270. In Stribild's most recent SmPC, Gilead states that for patients at risk, physician monitoring of creatinine clearance, serum phosphate, urine glucose, and urine protein more frequently than every four weeks during the first year of treatment and then every three months during Stribild therapy is "required."

271. Gilead has updated its Stribild EU labeling multiple times every year since 2013. Each time, Gilead determined that it should instruct doctors in the EU to monitor all

patients' kidneys on a frequent, specific schedule using multiple markers of kidney function, including serum phosphorus.

272. Unlike Gilead's U.S. labeling, Gilead's EU labeling for Viread and Truvada also discloses that a higher risk of renal impairment has been reported in patients receiving TDF as part of a ritonavir or cobicistat-boosted regimen (like Stribild), and doctors should carefully evaluate whether it is appropriate to prescribe TDF as part of a boosted regimen in patients with renal risk factors.

273. There is no medical, clinical, or scientific basis for the differences between the warnings contained in Gilead's labeling for its TDF-based products in the U.S. and its labeling for the same products in the EU. Gilead knew that it should instruct doctors to monitor all patients for multiple markers of kidney function on a frequent schedule but did not do so in the U.S.

274. Gilead was more concerned with increasing or maintaining TDF Drug sales in the U.S. by downplaying the safety risk and the need for careful, frequent monitoring of all patients than it was in safeguarding patients from the known risks of TDF toxicity.

275. In addition, until 2018, Gilead's U.S. warnings about the need to monitor patients for renal effects of Viread, Truvada, Atripla, and Complera were also far weaker than the warnings it gives to monitor patients for renal effects of TAF, even though TAF is far less toxic to kidneys than TDF. Gilead has consistently warned doctors to monitor all patients taking TAF-based drugs for multiple markers of renal function, including urine glucose and urine protein, not just estimated creatinine clearance.

276. For example, when the FDA approved Odefsey—the TAF version of Complera—on March 1, 2016, Gilead gave stronger monitoring warnings for safer Odefsey than it did for Complera, telling doctors that they should monitor all Odefsey patients, not just those at risk, for multiple markers of kidney function:

Complera's U.S. Label 03/01/2016	Odefsey's Labeling 03/01/2016
It is recommended that estimated creatinine clearance be assessed in all patients prior to initiating therapy and as clinically appropriate during therapy with COMPLERA. In patients at risk of renal dysfunction, including patients who have previously experienced renal events while receiving HEPSERA®, it is recommended that estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein be assessed prior to initiation of COMPLERA and periodically during COMPLERA therapy.	**Estimated creatinine clearance, urine glucose and urine protein should be assessed before initiating ODEFSEY therapy and should be monitored during therapy in all patients.** Serum phosphorus should be monitored in patients with chronic kidney disease because these patients are at greater risk of developing Fanconi syndrome on tenofovir prodrugs. Discontinue ODEFSEY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.[67]

277. When the FDA approved Descovy—the TAF version of Truvada—on April 4, 2016, Gilead gave stronger monitoring warnings for safer Descovy than it did for Truvada, telling doctors that they should monitor all Descovy patients, not just those at risk, for multiple markers of kidney function:

Truvada U.S. Labeling 04/04/2016	Descovy U.S. Labeling 04/04/2016
It is recommended that **estimated creatinine clearance be assessed in all individuals prior to initiating therapy and as clinically appropriate during therapy** with TRUVADA. In patients at risk of renal dysfunction, including patients	**Estimated creatinine clearance, urine glucose, and urine protein should be assessed before initiating DESCOVY therapy and should be monitored during therapy in all patients**. Serum phosphorus should be monitored in patients with

[67] On August 17, 2017, Gilead updated its Odefsey label to tell doctors to all monitor all patients, not just those with chronic kidney disease, for serum phosphorus.

Truvada U.S. Labeling 04/04/2016	Descovy U.S. Labeling 04/04/2016
who have previously experienced renal events while receiving HEPSERA®, it is recommended that estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein be assessed prior to initiation of TRUVADA, and periodically during TRUVADA therapy.	chronic kidney disease because these patients are at greater risk of developing Fanconi syndrome on tenofovir prodrugs. Discontinue DESCOVY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

278. Gilead determined that it should give stronger monitoring warnings for its safer TAF-based drugs, yet failed to strengthen its TDF Drug warnings for years.

2. Gilead failed to adequately warn patients about the risks of TDF.

279. Gilead failed to adequately warn patients about the risks of TDF, and the need to routinely monitor all patients taking TDF, in direct-to-consumer advertising and in patient labeling.

280. Gilead promoted its TDF Drugs directly to patients through direct-to-consumer advertising, including print and online media. Like its sales force's promotion to doctors, Gilead's consumer advertising downplayed the risks of TDF toxicity by, among other things, hiding risk information relative to the benefits of the drugs, and suggesting that kidney and bone adverse events only occurred in, and monitoring was only necessary for, patients with risk factors for such injuries.

281. For example, a print advertisement for Truvada that appeared in the November 2004 edition of *The Advocate*, the oldest and largest lesbian, gay, bisexual, and transgender magazine in the U.S., stated under the heading "Important Safety Information" that: "If you have had kidney problems or take other medicines that can cause kidney

problems, your medical professional should do regular blood tests to check your kidneys." Yet Gilead knew by this time that adverse kidney events were not limited to at risk patients, and thus should have warned doctors and patients about the need for frequent monitoring of all patients.

282. On March 26, 2010, the FDA issued another Warning Letter to Gilead, this time in connection with Gilead's direct-to-consumer print advertising for Truvada. The FDA stated that Gilead's Truvada advertisement was false and misleading because it overstated the efficacy of Truvada and minimized the risks associated with the drug, in violation of the Federal Food, Drug, and Cosmetic Act and FDA implementing regulations. The FDA noted that Truvada is associated with "serious risks" like new onset or worsening renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), and decreases in bone mineral density, including cases of osteomalacia (associated with proximal renal tubulopathy and which may contribute to fractures). The agency stated that Gilead's Truvada advertising was false or misleading because it failed to present the risks associated with Truvada with a prominence and readability comparable to the statements regarding the drug's benefits.

283. In addition to the reasons set forth in the Warning Letter, the Truvada advertising was also false and misleading because, like the earlier Truvada advertising, it continued to suggest that kidney problems only occurred in, and monitoring was also necessary for, patients that had had kidney problems in the past or took other medications that can cause kidney problems.

284. Upon information and belief, Gilead's other direct-to-consumer advertising for Viread, Truvada, Atripla, and Complera similarly failed to adequately warn patients about the true risk of TDF and the need to routinely monitor all patients for TDF-associated kidney and bone effects.

285. Gilead's patient package inserts for Viread, Truvada, Atripla, and Complera also failed to warn about all patients' need to be routinely monitored by their doctors for adverse kidney and bone effects. The patient package inserts said nothing for years about monitoring anyone other those who were already at risk for kidney and bone problems despite Gilead's knowledge that TDF was injuring patients without identified risk factors for such injuries.

286. Gilead's patient package inserts for Viread, Truvada, Atripla, and Complera failed to adequately warn patients even after Gilead had inadequately updated the warnings in its prescriber labeling.

287. For example, Gilead did not disclose to patients that Viread may cause "new or worse kidney problems" until more than two years after Gilead added that warning to the Viread prescriber labeling. And Gilead waited many more years before it added the "new or worse kidney problems" disclosure to the patient package inserts for other TDF products; it did not appear in the Truvada patient package insert until June 17, 2013 and did not appear in the Atripla patient package insert until July 25, 2018—nearly five and ten years respectively after Gilead first warned doctors that TDF may cause "new onset or worsening renal impairment."

288. Gilead similarly delayed disclosing to patients in the patient package inserts about doctors' need to assess all plaintiffs' kidney function prior to initiating treatment with TDF. Although Gilead added that warning to the Viread prescriber labeling in May 2007, it did not tell patients that "[y]our healthcare provider should do blood tests to check your kidneys before you start treatment" with TDF until August 16, 2012, for Viread, May 15, 2018, for Truvada, July 25, 2018, for Atripla, and January 25, 2013, for Complera. At a minimum, Gilead was grossly negligent in failing to ensure that its warnings to patients were consistent with those it gave to doctors and the patient warnings it gave were consistent among its various TDF Drugs.

3. Gilead could have unilaterally strengthened its TDF drug labels.

289. Gilead could have strengthened the Warnings, Precautions, and Adverse Events sections of the labels for its TDF Drugs unilaterally without prior FDA approval.

a. Gilead could have unilaterally strengthened its warnings before FDA approval.

290. Each time Gilead sought FDA approval for a new TDF Drug, it could have strengthened its label before the drug obtained FDA approval. Gilead bears primary responsibility for its drug labeling at all times, and was responsible for crafting adequate labels before the drugs were FDA approved. No federal law prevented Gilead from submitting a stronger warning label to the FDA prior to the initial approval of the TDF Drugs. And the FDA would not have prevented Gilead from strengthening its monitoring warnings in advance of FDA approval.

291. Gilead's initial EU label for its first TDF Drug, Viread, included stronger monitoring warnings. As it did in the EU, Gilead could have included stronger warnings in its initial Viread label in the U.S.—had Gilead been concerned with patient safety rather than U.S. sales.

292. Moreover, before Gilead submitted Truvada, Atripla, Complera, and Stribild for FDA approval in the U.S., it knew that it gave stronger monitoring warnings for its TDF Drugs in the EU. Gilead knew, as evidenced by its EU labels, that stronger warnings were warranted. It could have and should have used this knowledge to strengthen its U.S. labels.

293. In addition, once TDF was on the market, each time Gilead submitted a new TDF Drug for FDA approval, it did so with years of cumulative knowledge as to the adverse toxic effects of TDF. Faced with accumulating information about adverse kidney and bone toxicity, including in patients without preexisting risk factors, Gilead could have strengthened its monitoring warnings before submitting the drugs for FDA approval.

294. The FDA would not have rejected Gilead's stronger warnings. The FDA has, in fact, approved labels including stronger monitoring warnings for the TDF Drugs, as well as the safer TAF drugs.

b. Gilead could have unilaterally strengthened its warnings after FDA approval.

(1) Before August 22, 2008

295. Prior to August 22, 2008, Gilead could have strengthened its Viread, Truvada, and Atripla labels via CBE without prior FDA approval. Under the CBE

regulation in effect during that time, Gilead could have simply submitted a supplemental submission strengthening the labels' warnings and/or its instructions about the safe administration of the drugs. 21 C.F.R. § 314.70(c)(6)(iii).

296. Among other things, Gilead could have strengthened the labels' warnings by providing additional information about laboratory tests helpful in following the patient's response or identifying possible adverse reactions, including such factors as the range of normal and abnormal values and the recommended frequency with which tests should be performed before, during, and after therapy. 21 C.F.R. § 201.57(c)(6).

297. Prior to August 22, 2008, Gilead could have strengthened its labels via CBE without regard to whether it possessed information that it did not previously provide to the FDA.

298. The FDA would not have rejected Gilead's supplemental submission to strengthen the TDF labels. The FDA has, in fact, approved labels including stronger monitoring warnings for the TDF Drugs, as well as the safer TAF drugs.

(2) On and after August 22, 2008 through July 2012

299. On and after August 22, 2008, when the CBE regulation was amended, Gilead could have unilaterally strengthened its labels for Viread, Truvada, Atripla, and Complera post-FDA approval based on "newly acquired information," *i.e.*, information that was not previously presented to the FDA.

300. Gilead could have strengthened the Warnings, Precautions, and Adverse Events sections of its labels unilaterally, without requiring prior FDA approval, based on,

among other things: increasing post-approval evidence that patients with and without preexisting risk factors were experiencing kidney and bone adverse effects with a frequency greater than reported in Gilead's clinical trials; expanding post-approval evidence that all patients are at risk for TDF-induced nephrotoxicity, meaning that doctors should monitor all patients for multiple indicators of renal function, including tubular dysfunction; and Gilead's own post-approval determinations to give stronger warnings regarding the exact same TDF Drugs in the EU.

301. Except for Stribild, Gilead's clinical trials of the TDF Drugs, upon which FDA approval was based, did not show significant nephrotoxicity of TDF, despite preclinical evidence demonstrating that TDF could be highly toxic to kidneys and bones. However, once Gilead started marketing TDF, patients quickly began experiencing TDF's nephrotoxic effects, some severe and irreversible. Although the FDA became aware, after the clinical trials through adverse event reporting, that TDF was injuring patients' kidneys and bones, it did not know the true frequency or severity of adverse events, injury, or risk associated with TDF.

302. On May 21, 2007, Gilead changed its Viread label to instruct doctors to calculate creatinine clearance in all patients before initiating treatment with TDF and as clinically appropriate during therapy. Gilead recommended the monitoring of creatinine clearance and serum phosphorus only for patients at risk of renal impairment.

303. This warning remained inadequate because it failed to instruct doctors to frequently monitor all patients for sufficiently sensitive markers of kidney function that

could detect early signs of nephrotoxicity and thus prevent or lessen the harm of TDF. As Gilead had known since at least 2002, TDF was injuring patients with no preexisting risk factors for kidney impairment. Gilead's May 21, 2007 label change perpetuated the false distinction between patients "at risk" for TDF-induced nephrotoxicity and everyone else. But as subsequent studies would make clear, while there may be certain factors that increase a patient's risk of TDF-induced renal damage, *all TDF patients are at risk*—making frequent, careful monitoring of all patients essential for safe use of the drug.

304. As clinicians' experience with TDF grew, the medical literature recognized that even if TDF may not frequently impair kidneys' *glomerular function*—as measured by serum creatinine or creatinine clearance—in the absence of established risk factors, TDF-induced damage to kidneys' *tubular function* is much more common and cannot be adequately predicted by traditional risk factors for kidney impairment or detected by monitoring for glomerular function. These new studies demonstrated a heightened risk to all patients, leading study authors to conclude that all patients must be frequently monitored for markers of tubular function—e.g., serum phosphorus, in addition to creatinine clearance.

305. For example, the 2009 paper, Labarga P., *et al*., "Kidney tubular abnormalities in the absence of impaired glomerular function in HIV patients treated with tenofovir," described the study of glomerular and tubular function in 284 patients, 154 of whom took TDF, 49 of whom took another HIV regimen, and 81 of whom took no antiretroviral drugs. The authors found that glomerular function, as measured by plasma

creatinine levels or creatinine clearance or both, was within normal limits and comparable among all study groups. Tubular dysfunction, on the other hand, was far more frequent in the TDF group (22%), as compared to those never treated with TDF (6%) or never exposed to antiretrovirals (12%). The authors also identified three TDF patients with complete Fanconi syndrome (the signature TDF toxicity), even though each patient's creatinine clearance was within the normal range. After follow-up, the data showed that the TDF patients had a significantly greater risk for tubular damage than patients never treated with TDF: an estimated 25% rate of tubular dysfunction at 4 years for TDF patients compared to null for the rest.

306. The Labarga study also found that no risk factor other than TDF use and old age was predictive of tubular dysfunction. And because estimates of glomerular function like creatinine clearance were not predictive of tubular function, the authors explained that unless tubular parameters like urine glucose and/or phosphorus are routinely monitored, tubular abnormalities may go undiagnosed. And if tubular damage persists unnoticed, patients may progress to more severe kidney damage and experience a chronic loss of phosphorus, leading to bone mineral density loss and premature osteoporosis. The authors recommended that all TDF patients be monitored for signs of tubular damage so that a switch in therapy could be considered in the event of progressive deterioration.

307. A 2011 article, Hall AM *et al*., "Tenofovir-associated kidney toxicity in HIV-infected patients: a review of the evidence," conducted a literature review and further addressed the disconnect between results of studies examining markers of glomerular

function with the nephrotoxicity seen in practice. The authors noted that prior studies tended to establish that TDF was not often significantly toxic to the glomerulus—which contrasted with the authors' clinical experience in treating TDF patients for nephrotoxicity. In practice, TDF-associated nephrotoxicity was the authors' most common reason for referral of HIV patients to specialist renal services. The authors explained that the main site of TDF toxicity was the proximal renal tubule (not the glomerulus) and that proximal tubule dysfunction may not be detected by measuring glomerular filtration.

308. Because (a) TDF-associated nephrotoxicity can occur in patients without obvious risks factors and at highly variable times after the initiation of therapy, and (b) standard tests of glomerular function are insufficiently sensitive to detect early or mild cases of nephrotoxicity, the authors concluded that all patients on TDF should be carefully and routinely monitored (every 3 months during the first year then twice yearly) for signs of both glomerular and tubular dysfunction so that long-term effects on kidney and bone health can be assessed.

309. A 2012 paper, Scherzer, R., *et al.*, "Association of Tenofovir Exposure with Kidney Disease Risk in HIV Infection," discussed the authors' study of 10,841 HIV-infected patients from the Veterans Health Administration to assess the associations of tenofovir with kidney disease outcomes. The authors found that each year of tenofovir exposure was associated with a 34% increased risk of proteinuria, 11% increased risk of rapid decline in kidney function, and 33% increased risk of chronic kidney disease. The results provided "strong evidence that tenofovir may cause clinically significant toxicity to

the kidney that is not reversible." The study also demonstrated that traditional risk factors did not worsen the effects of tenofovir. The authors concluded that "while traditional risk factors such as hypertension, older age, and diabetes may increase the risk for kidney disease, tenofovir is associated with elevated risk even in patients without preexisting risk factors."[68]

310. The authors explained the strength of their results in light of the study's large patient population and inclusion of patients who are often excluded from clinical trials or do not qualify or volunteer for cohort studies. The authors contrasted their study with the design of previous studies which made them less able to detect statistically significant associations between tenofovir use and kidney disease.

311. A 2013 paper, Reynes, J., *et al.*, "Tubular and glomerular proteinuria in HIV-infected adults with estimated glomerular filtration rate ≥60 ml/min per 1.73," recommended that all TDF patients be systematically monitored for markers of tubular injury in light of the authors' finding that nearly 20% of 1200 patients had proteinuria even though they had a normal creatinine-based estimated glomerular filtration rate.

312. And a 2014 paper, Bonjoch, A., *et al.*, "High prevalence of signs of renal damage despite normal renal function in a cohort of HIV-infected patients: evaluation of

[68] The FDA cited the Scherzer study in connection with its medical review of the Stribild NDA in July 2012. At most, this demonstrates the FDA's knowledge of this study as of July 2012—approximately 4 years after the CBE regulation requiring "newly acquired information" became effective. Plaintiffs do not assert post-FDA approval failure to warn claims with respect to Stribild.

associated factors," also found that signs of renal damage were "highly frequent" even in patients with a normal estimated glomerular filtration rate. The authors concluded that the data demonstrated the need for early detection of renal injury, even in patients with normal renal function.

313. These papers, and others in this timeframe that demonstrated a high percentage of TDF patients with proximal renal tubular dysfunction, stand in stark contrast to Gilead's Viread clinical trials and subsequent attempts to maintain that only some TDF patients are at risk. Unlike the Viread clinical trials, these papers showed significant nephrotoxicity of TDF—with toxicity occurring at a high frequency and high risks of kidney disease outcomes looming even in patients with normal glomerular function and without traditional risk factors.

314. The clinical trials reported that the frequency of renal events leading to drug discontinuation was low (0.4%). Despite these results, Gilead knew that the potential for TDF to be toxic was high, particularly in real world settings over the long-term. And, indeed, multiple retrospective studies have demonstrated that the rate of renal adverse events leading to drug discontinuation was many times higher than what was reported in clinical trials. For example, the 2011 paper, "Tenofovir-induced renal toxicity in 324 HIV-infected antiretroviral-naïve patients," found that drug discontinuation due to decline in GFR or tubular dysfunction was 9.2%.

315. Postmarketing adverse event reports did not put the FDA on notice of the frequency or severity of the risk. Adverse event reports underreport the true incidence of

adverse events because they are based on voluntary reporting. And they do not reflect the damage TDF inflicts on kidneys and bones before renal function declines, the risk of future adverse kidney or bone outcomes, nor the benefits of frequent, careful monitoring of all patients for early signs of nephrotoxicity as demonstrated by these new studies.

316. Further, there is no evidence that Gilead submitted to the FDA analyses demonstrating that TDF patients have a high frequency of renal damage or the true extent of the risk nephrotoxicity poses to all TDF patients even if they have normal glomerular function or do not have preexisting risk factors.

317. Gilead did not submit analyses to the FDA establishing the full extent of the frequency or severity of risk that TDF poses to all patients, nor did it tell the FDA that the one marker of kidney function Gilead was warning doctors to monitor in all patients after May 21, 2007 could not adequately detect the type of kidney injury that was frequently occurring in all TDF patients (and, which left unchecked, would cause more severe kidney injury and also harm patients' bones). Gilead could have analyzed the accumulating data demonstrating the higher frequency and severity of the risk to all TDF patients and strengthened its warnings, but did not.

318. Until the FDA's review of the Stribild NDA in 2012, there is no evidence that the agency reviewed any medical literature regarding TDF or other analyses describing how post-approval renal and bone injury and/or adverse events were occurring at a frequency or severity much greater than that reported in the registrational clinical trials. The FDA based its approval of Viread on the preclinical data and clinical trials Gilead

submitted in its Viread NDA. After Viread was approved, the FDA based its approvals of the Truvada, Atripla, and Complera NDAs on Gilead's data showing the bioequivalence of those combination drugs to their individual components. The FDA's approvals of Truvada, Atripla, and Complera were not based on any new clinical studies or other analyses regarding safety of TDF. When the FDA conducted a more searching review in connection with the Stribild NDA, Gilead proposed and the FDA approved stronger monitoring warnings for Stribild, which included recommending the monitoring of all patients for glomerular and tubular injury.

319. Unlike in the U.S., Gilead did warn—since 2002—physicians in the EU to frequently monitor all patients for both glomerular (creatinine clearance) and tubular (serum phosphorus) injury. In fact, after Gilead received FDA approval to market each of the TDF Drugs, it repeatedly determined to give stronger monitoring warnings for the exact same TDF Drugs in the EU. Upon information and belief, Gilead did not disclose to the FDA that it gave stronger monitoring warnings in the EU for the exact same products nor did it disclose its scientific or medical reasons for doing so.

320. In addition, once Gilead finally launched the safer TAF-based drugs (after approval of the TDF Drugs) it also gave stronger monitoring warnings for the safer TAF drugs than it gave in the TDF Drugs' labels, including recommending that doctors monitor all patients for both glomerular and tubular injury.

321. The FDA would not have rejected a label change strengthening monitoring recommendations to protect all patients from risks of TDF-induced kidney and bone

adverse effects. In 2018, the FDA did, in fact, approve labels including stronger monitoring warnings for Viread, Truvada, Atripla, and Complera, like it did for the safer TAF drugs years earlier.

V. TOLLING OF THE STATUTE OF LIMITATIONS

322. Gilead misrepresented that TAF was "new" despite knowing that it had discovered the benefits of TAF even before Viread was approved in 2001.

323. Gilead misrepresented the reasons that it shelved TAF in 2004, asserting that TAF could not be differentiated from TDF when it knew that TAF was, in fact, highly differentiated from TDF.

324. Gilead concealed that it shelved TAF in 2004 in order to extend the lifecycle of its HIV product portfolio while patients were injured by TDF-induced kidney and bone toxicity.

325. Gilead misrepresented that it renewed development of TAF because of the needs of an aging HIV population. Gilead knew by 2004 when it halted TAF development that, as a result of cART, many HIV patients had a normal life expectancy.

326. For years, Gilead has publicized the pretext for its decision to halt and then renew TAF development in order to conceal the existence of Plaintiffs' claims.

327. Gilead concealed that it did not reduce the dose of TDF in Stribild even though it knew to reduce the tenofovir prodrug dose when combined with cobicistat.

328. Gilead concealed the true risk of kidney and bone injuries TDF posed to patients who did not have preexisting risk factors for such injuries and concealed from U.S.

doctors and patients what it knew about the need to monitor all patients for TDF associated toxicity.

329. Because of Gilead's misrepresentations and omissions, plaintiffs did not know and had no reason to suspect that Gilead's wrongdoing was the cause of their injuries and could not have discovered their claims.

330. No reasonable person taking TDF-based drugs and experiencing kidney and bone toxicities would have suspected that Gilead purposefully withheld a safer design that would have ameliorated those very side effects.

331. No reasonable person without prior risk factors for renal or bone harm taking TDF-based drugs and experiencing kidney and bone toxicities would have suspected that Gilead failed to adequately warn them because the label misleadingly suggests that only patients with preexisting risk factors were in danger.

332. No reasonable person would have suspected that Gilead provided stronger warnings to patients and doctors in the EU than it did in the U.S. for the exact same TDF products.

333. Gilead's misrepresentations and omissions would lead a reasonable person to believe that he or she did not have a claim for relief.

334. Because of Gilead's misrepresentations and omissions, neither Plaintiffs nor any reasonable person would have had reason to conduct an investigation. Once Plaintiffs suspected that Gilead's wrongdoing was the cause of their injuries, they were diligent in trying to uncover the facts.

335. Gilead's misrepresentations and omissions regarding its refusal to earlier market TAF-designed products and the true risks of TDF constitute continuing wrongs that continue to this day.

VI. CLAIMS FOR RELIEF

COUNT I

NEGLIGENCE AND GROSS NEGLIGENCE

336. Plaintiffs reallege and incorporate the allegations made above as if fully set forth below.

337. Gilead has a duty to exercise ordinary care in the design, manufacture, marketing, and sale of its pharmaceutical products, including the TDF Drugs.

338. Gilead has a duty to refrain from selling unreasonably dangerous products, including the duty to ensure that its pharmaceutical products do not cause patients to suffer from foreseeable risks of harm.

339. Gilead has a duty to monitor the adverse effects associated with its pharmaceutical products, including the TDF Drugs.

340. Gilead has a continuing duty to warn of the adverse effects associated with its pharmaceutical products, including the TDF Drugs, to avoid reasonably foreseeable risks.

341. Gilead has a duty to identify any laboratory tests helpful in identifying adverse reactions and the recommended frequency with which such tests should be performed.

342. Gilead has a duty to exercise reasonable care when it undertakes affirmative acts for the protection of others.

343. Gilead owes these duties to Plaintiffs because it was foreseeable to Gilead that patients like Plaintiffs would ingest and consequently be endangered by its TDF Drugs.

344. Gilead knew that the TDF design it incorporated into the TDF Drugs was associated with risks of kidney and bone toxicity and caused injuries that resulted from kidney and bone toxicity—including in patients not otherwise at risk for such injuries. Gilead's knowledge that TDF harmed patients' kidneys and bones only grew with each year TDF was on the market. By the time Stribild entered the market, Gilead had more than a decade's worth of knowledge that TDF was toxic to kidneys and bones.

345. Gilead knew that combining 300 mg of TDF with cobicistat resulted in even greater toxicity, and that it could reduce the tenofovir prodrug dose when combined with cobicistat and achieve the same therapeutic effects. Despite this knowledge, Gilead did not reduce the TDF dose in Stribild.

346. Gilead knew, before its first TDF Drug and every subsequent TDF Drug was approved by the FDA, that TAF is safer than TDF in that it reduces the risks of kidney and bone toxicities associated with TDF. Despite knowing that TAF would reduce foreseeable harm to patients' kidneys and bones, Gilead repeatedly incorporated the TDF design into the TDF Drugs prior to FDA approval and prevented patients from taking a safer TAF-based product so Gilead could make more money.

347. Based, *inter alia*, on its duty to monitor the adverse effects associated with Viread, Truvada, Atripla, Complera, and Stribild, Gilead knew that the likelihood and severity of the harm associated with TDF was great. Thousands of patients experienced damage to their kidneys and bones as a result of TDF exposure—some of it severe and irreversible. The likelihood and severity of the kidney and bone injuries suffered by patients like Plaintiffs far outweighed Gilead's burden in taking safety measures to reduce or avoid the harm. Gilead had already designed the safer TAF method of introducing tenofovir into the body before it sought FDA approval for the TDF Drugs. Gilead had also reduced the TAF dose when combined with cobicistat in Genvoya, when it was developing Stribild.

348. Gilead failed to exercise ordinary care in the design, manufacture, and sale of the TDF Drugs.

349. Gilead failed to use the amount of care in designing the TDF Drugs that a reasonably careful manufacturer would have used before FDA approval to avoid exposing patients to foreseeable risks of harm.

350. Gilead undertook to develop and market a safer TAF-designed product to sell to wholesalers and other direct purchasers of pharmaceuticals. Gilead recognized that its development and marketing of safer TAF-designed products was for the protection of patients like Plaintiffs. By shelving the safer TAF design purely for monetary gain and deceptively representing why it was abandoning the safer TAF design, Gilead failed to exercise reasonable care in the performance of this undertaking that increased the risk of

harm to patients like Plaintiffs. Gilead's failure to exercise reasonable care resulted in physical harm to Plaintiffs.

351. Gilead failed to use the amount of care in warning about the risks and safe use of the TDF Drugs that a reasonably careful manufacturer would have used to avoid exposing patients to foreseeable risks of harm.

352. Gilead knew or reasonably should have known that the TDF Drugs were dangerous or likely to be dangerous when used in a reasonably foreseeable manner.

353. Gilead knew or reasonably should have known that Plaintiffs and Plaintiffs' physicians would not realize the danger posed by inadequate monitoring of patients taking TDF Drugs.

354. Gilead failed to adequately warn Plaintiffs and Plaintiffs' physicians about the need to monitor all patients taking the TDF Drugs. For years, Gilead failed to recommend that doctors monitor anyone other than patients "at risk" for TDF-induced kidney and/or bone injuries. When Gilead finally added a weak instruction regarding the monitoring of all patients for kidney damage, it only warned doctors to monitor patients for one insufficient marker of kidney dysfunction that was incapable of detecting many dangerous changes in kidney dysfunction, and failed to warn doctors to monitor TDF patients on a frequent schedule. Gilead's monitoring warnings with respect to "at risk" Viread, Truvada, Atripla, Complera, and Stribild users were also inadequate because they failed to warn doctors to monitor patients on a specific, frequent schedule.

355. Gilead could have unilaterally strengthened its U.S. labels before FDA approval for all TDF Drugs and after FDA approval for Viread, Truvada, Atripla, and Complera through July 2012.

356. A reasonable manufacturer and seller under the same or similar circumstances would have instructed Plaintiffs and Plaintiffs' physicians on the safe use of the TDF Drugs, i.e., use where doctors frequently monitored all TDF patients for TDF-associated toxicity, including monitoring for kidney damage using more than one inadequate test. Gilead knew to warn doctors to frequently monitor all patients for kidney damage using more than one inadequate test because it did so in the European Union.

357. Gilead's failure to adequately warn Plaintiffs and Plaintiffs' doctors about the need to monitor TDF Drug patients was compounded by Gilead's omissions to doctors during sales detailing and other promotional activities. Gilead's misleading promotion of the TDF Drugs undermined the efficacy of its existing (inadequate) warnings.

358. Plaintiffs were injured by using TDF in a reasonably foreseeable way.

359. The lack of adequate warnings was a substantial factor in causing Plaintiffs' injuries.

360. Had Gilead adequately warned Plaintiffs' doctors, Plaintiffs' doctors would have read and heeded such adequate warnings.

361. Plaintiffs' properly warned physicians would have monitored Plaintiffs differently—by frequently monitoring Plaintiffs using sufficiently sensitive markers of kidney function that would have alerted doctors to early signs of nephrotoxicity, including

tubular damage that leads to more severe renal adverse events and bone mineral density loss. Once they recognized the signs of nephrotoxicity, Plaintiffs' physicians would have taken further action after weighing their treatment options, such as increased monitoring, less frequent dosing, or drug discontinuation, before the damage manifested, worsened, or became irreversible. Plaintiffs' properly warned physicians would have detected TDF toxicity earlier, thus preventing or lessening Plaintiffs' injuries.

362. Plaintiffs were injured as a direct and proximate result of Gilead's negligence.

363. Gilead's conduct constitutes gross negligence and willful misconduct.

364. By designing the TDF Drugs to contain TDF when it knew TDF harmed patients' kidneys and bones, and intentionally withholding the safer TAF design from patients, while failing to adequately warn of the known risks and safe use of TDF, Gilead acted in reckless disregard of, or with a lack of substantial concern for, the rights of others. By designing Stribild to contain 300 mg TDF when it knew to reduce the tenofovir prodrug dose with combined with cobicistat, Gilead acted in reckless disregard of, or with a lack of substantial concern for, the rights of others.

365. Gilead intentionally designed the TDF Drugs to contain 300 mg TDF and withheld the safer designs from patients while in disregard of the known risk of TDF-induced kidney and/or bone toxicity, making it highly probable that harm would result.

366. Gilead knew that its conduct would harm patients like Plaintiffs but Gilead withheld its safer designs to make more money.

COUNT II

FRAUD BY OMISSION

367. Plaintiffs reallege and incorporate the allegations made above as if fully set forth below.

368. Gilead has a duty to exercise ordinary care in the design, manufacture, marketing, and sale of its pharmaceutical products, including the TDF Drugs.

369. Gilead has a duty to refrain from selling unreasonably dangerous products, including the duty to ensure that its pharmaceutical products do not cause patients to suffer from foreseeable risks of harm.

370. Gilead has a duty to monitor the adverse effects associated with pharmaceutical products, including Stribild.

371. Gilead has a duty to exercise reasonable care when it undertakes affirmative acts for the protection of others.

372. Gilead owes these duties to Plaintiffs because it was foreseeable to Gilead that patients like Plaintiffs would ingest and consequently be endangered by the TDF Drugs.

373. Gilead also owed a duty to speak because it was in possession of information about TDF and TAF that was not readily available to Plaintiffs and Plaintiffs' physicians, made partial representations about TDF and TAF to Plaintiffs and Plaintiffs' physicians while suppressing material facts, and actively concealed material information about TDF and TAF from Plaintiffs and Plaintiffs' physicians, including that: (a) Gilead knew about

the safer TAF design for delivering tenofovir into the body prior to seeking and receiving FDA approval for the TDF Drugs but designed the TDF Drugs to include TDF anyway, even though it knew that TDF posed a significant and increased safety risk to patients' kidneys and bones; (b) the toxicity associated with tenofovir was not unavoidable; (c) the real reason Gilead abandoned its TAF design in 2004 was not because TAF could not be sufficiently differentiated from TDF; (d) Gilead had already determined that it should reduce the dose of tenofovir prodrug when combining it with cobicistat at the time it was developing Stribild but Gilead did not reduce the TDF dose in Stribild as it did with Genvoya; (e) Gilead purposefully withheld the TAF design, which it knew was safer than TDF, solely to make more money; and (f) Gilead knew to warn doctors to frequently monitor all patients for the adverse effects of TDF toxicity using more than one insufficient marker of kidney function even though it did not do so in its warnings to doctors in the U.S.

374. Gilead knew that this information was not readily available to Plaintiffs and their doctors, and Plaintiffs and their doctors did not have an equal opportunity to discover the truth. Plaintiffs and their doctors had no practicable way of discovering the true state and timing of Gilead's knowledge.

375. Gilead intentionally omitted adequate warnings about the risks and safe use of TDF when promoting the TDF Drugs to doctors and patients by, *inter alia*, omitting information about the frequency and severity of adverse kidney and bone events and failing to tell doctors to adequately monitor TDF patients for drug-induced toxicity.

376. Gilead intentionally omitted from its prescriber and patient labeling an adequate warning regarding the need for doctors to monitor all TDF patients, on a frequent, specific schedule, for the adverse effects of TDF-associated bone and kidney toxicity. Gilead intentionally omitted an adequate monitoring warning in order to conceal the true risk of its TDF-based antiviral products, and to inflate sales by inducing doctors to prescribe, and patients like Plaintiffs to consume, its TDF Drugs. Gilead could have unilaterally strengthened its U.S. labels before FDA approval for all TDF Drugs and after FDA approval for Viread, Truvada, Atripla, and Complera through July 2012.

377. By providing inadequate warnings that were contrary to those it gave with respect to the exact same drugs in the EU, Gilead partially disclosed material facts. Gilead had a duty of complete disclosure once it began to speak.

378. Plaintiffs and their doctors justifiably relied on Gilead's product labeling and other representations.

379. Had Gilead not omitted this information about the safe use of its drugs from the prescriber and patient labeling, doctors would have performed, and patients would have insisted upon, frequent and adequate monitoring for the kidney and bone problems that have injured Plaintiffs. But for Gilead's omissions, Plaintiffs would have consumed the TDF Drugs in a safer way.

380. If Plaintiffs had been adequately monitored for kidney and bone problems while taking TDF, they would not have been injured or their injuries would have been less severe.

381. Gilead intentionally concealed from Plaintiffs and their doctors the fact that Gilead had already developed the safer TAF mechanism but designed the TDF Drugs to contain TDF instead of the safer TAF design in order to maximize profits on its TDF-based products and extend its ability to profit on its HIV franchise for years to come.

382. Gilead also intentionally concealed from Plaintiffs and their doctors that Gilead knew that the tenofovir prodrug dose should be reduced when combined in a fixed dose combination pill with cobicistat, but did not reduce the TDF dose in Stribild as it did with Genvoya.

383. By concealing that Gilead was aware of but had withheld the safer designs, Gilead intended to and did induce Plaintiffs' doctors to prescribe, and Plaintiffs to ingest, one or more of the TDF Drugs, thereby causing Plaintiffs' injuries.

384. Plaintiffs and their doctors justifiably relied on Gilead's omissions regarding TAF.

385. Had Gilead disclosed that it was aware of, but intentionally withheld, the safer TAF mechanism for delivering tenofovir into the body, Plaintiffs would have ingested TDF in a safer manner.

386. Plaintiffs' doctors would have ensured that Plaintiffs ingested TDF in a safer manner through increased and/or more careful monitoring for TDF-induced kidney and bone toxicity, or by prescribing TDF without coadministration with cobicistat.

387. Plaintiffs were injured as a direct and proximate result of Gilead's material omissions.

COUNT III

BREACH OF IMPLIED WARRANTY OF MERCHANTABILITY

388. Plaintiffs reallege and incorporate the allegations made above as if fully set forth below.

389. Gilead is the manufacturer and seller of the TDF Drugs.

390. An implied warranty of fitness for human consumption runs from Gilead to consumers like Plaintiffs.

391. Gilead impliedly warranted to Plaintiffs and their doctors that the TDF Drugs were of merchantable quality, and fit and safe for the use for which they were intended.

392. Plaintiffs ingested the TDF Drugs for the treatment of HIV, Hepatitis B, or PrEP, which is the purpose for which the drugs were manufactured, sold, and prescribed.

393. Plaintiffs relied on Gilead's skill or judgment to provide a product suitable for this purpose. Gilead is in the business of designing, manufacturing, selling, and marketing prescription drugs and specializes in drugs for the treatment or prevention of HIV, and treatment of Hepatitis B.

394. Gilead had reason to know that Plaintiffs and their doctors would rely on Gilead's skill or judgment.

395. The TDF Drugs are unfit for the purpose for which they were purchased because they are toxic to patients' kidneys and bones when put to their intended and ordinary use, causing injuries to Plaintiffs.

396. The dangers the TDF Drugs posed to Plaintiffs' kidneys and bones were known and knowable to Gilead at the time of manufacture and sale. Yet Gilead marketed the TDF Drugs without adequate warnings about the risks or safe use of TDF of which it knew or should have known.

397. Plaintiffs suffered kidney and/or bone injuries as a result of ingesting the TDF Drugs.

398. In addition to the common law, the conduct alleged herein constitutes a breach of the implied warranty of merchantability under the Uniform Commercial Code as codified in N.C. Gen. Stat. Ann. §25-2-314.

399. On January 12, 2022, Plaintiffs sent a letter to Gilead via certified mail giving official notice of Gilead's breach of the implied warranty of merchantability under the laws of North Carolina. Plaintiffs' notice letter is attached as Exhibit A.

COUNT IV

VIOLATION OF STATE CONSUMER PROTECTION LAWS

400. Plaintiffs reallege and incorporate the allegations made above as if fully set forth below.

401. Plaintiffs are consumers within the meaning of North Carolina's consumer protection laws because they are natural persons who purchased one or more of the TDF Drugs for personal, family, or household use.

402. The TDF Drugs are goods and merchandise within the meaning of the North Carolina consumer protection laws.

403. Gilead manufactured, sold, and marketed its TDF Drugs in trade or commerce, including within each of the 50 U.S. States.

404. Gilead engaged in unconscionable, unfair, false, fraudulent, misleading, and deceptive acts and practices in connection trade or commerce involving its TDF Drugs.

405. Gilead engaged in unfair and/or unconscionable conduct by knowingly designing its TDF Drugs to be unreasonably dangerous before FDA approval and withholding the safer designs to make more money.

406. Gilead also intentionally suppressed, concealed, and omitted material facts about the risks and benefits of the TDF Drugs in its promotional, marketing, and/or labeling communications to Plaintiffs and Plaintiffs' doctors, including, but not limited to: (1) the true frequency and severity of the risks of TDF to kidneys and bones; (2) that all TDF patients should be carefully monitored for adverse kidney and bone effects on a frequent schedule in light of the true risks of TDF; (3) that Gilead had already developed the safer TAF design for delivering tenofovir into the body but nevertheless designed the TDF Drugs to contain TDF, and withheld the safer TAF design, in order to avoid admitting the toxicity of TDF, maximize profits on its TDF-based products, and extend its ability to profit on its HIV franchise for years to come; and (4) Gilead knew that the tenofovir prodrug dose should be reduced when combined in a fixed dose combination pill with cobicistat, but did not reduce the TDF dose in Stribild.

407. Gilead had a duty to disclose the omitted material facts about TDF and TAF because it: (a) was in possession of information about TDF and TAF that was not readily

available to Plaintiffs and Plaintiffs' physicians; (b) made partial representations about TDF and TAF to Plaintiffs and Plaintiffs' physicians while suppressing material facts; and (c) actively concealed material information about TDF and TAF from Plaintiffs and Plaintiffs' physicians.

408. Gilead's conduct significantly impacted the public as actual or potential consumers of Gilead's TDF Drugs. Hundreds of thousands of consumers in the U.S. have ingested one or more of the TDF Drugs and Gilead has directed its misleading marketing and promotional messages to the market generally. Consumers like Plaintiffs are at an informational disadvantage and lack bargaining power relative to Gilead. Gilead's conduct has previously impacted other consumers and has significant potential to do so in the future.

409. Gilead's conduct was likely to mislead and did mislead reasonable consumers and members of the public.

410. Gilead's omissions were material and affected Plaintiffs' and Plaintiffs' doctors' conduct.

411. Gilead intended that others rely on its deceptive and misleading omissions regarding its TDF Drugs.

412. Plaintiffs and their doctors reasonably relied on Gilead's deceptive and misleading omissions regarding its TDF Drugs.

413. Plaintiffs' doctors prescribed, and Plaintiffs ingested, one or more of the TDF Drugs in reliance on Gilead's unconscionable, false, misleading and/or deceptive acts and omissions.

414. Plaintiffs were directly and proximately injured as a result of Gilead's deceptive conduct. But for Gilead's unfair and/or unconscionable conduct, Plaintiffs would have ingested a safer tenofovir-prodrug product, thus preventing or reducing Plaintiffs' injuries and monetary expenses in connection with taking TDF. But for Gilead's omissions, Plaintiffs would have ingested the TDF Drugs in a safer way—through more careful, frequent monitoring and/or by not taking Stribild (TDF in combination with cobicistat)—thus preventing or reducing Plaintiffs' injuries and monetary expenses in connection therewith.

415. Plaintiffs suffered ascertainable losses as a result of Gilead's violations North Carolina, N.C. Gen. Stat. §§ 75-1.1 *et seq*.

416. Gilead's conduct constitutes unfair methods of competition and unfair or deceptive acts or practices in or affected commerce in violation of N.C. Gen. Stat. §§ 75-1.1 *et seq*.

417. Plaintiffs could not discover the truth by exercise of reasonable diligence and they were induced to forego any investigation by Gilead's misrepresentations.

418. Gilead's violations of N.C. Gen. Stat. §§ 75-1.1*et seq* proximately caused Plaintiffs' injuries.

419. Plaintiffs seek actual damages, treble damages, and attorneys' fees in light of Gilead's willful violations.

PRAYER FOR RELIEF

Wherefore, Plaintiffs request that the Court enter an order or judgment against Gilead and in favor of Plaintiff, and grant the following relief:

A. Declare, adjudge, and decree the conduct of Gilead as alleged herein to be unlawful, unfair, and/or deceptive and otherwise in violation of the law;

B. Award Plaintiffs actual, compensatory, and/or statutory damages in an amount to be proven at trial;

C. Award Plaintiffs punitive and exemplary damages as permitted by law and the statutes cited herein in an amount to be proven at trial;

D. Award Plaintiffs restitution and restitutionary disgorgement to restore ill-gotten gains received by Gilead as a result of the unfair, wrongful, and deceptive conduct alleged herein;

E. Award Plaintiffs the costs of bringing this suit, including reasonable attorneys' fees; and

F. Award Plaintiffs such other and further relief as to which Plaintiffs may be entitled in law or equity.

JURY DEMAND

Pursuant to Federal Rule of Civil Procedure 38(c), Plaintiffs demand a trial by jury on all matters so triable.

DATED: January 18, 2022

Respectfully submitted,

HILLARD MARTINEZ GONZALES LLP

By: */s/ Emily J. Beeson*

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