IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

VIIV HEALTHCARE COMPANY, SHIONOGI & CO., LTD., and VIIV HEALTHCARE UK (NO. 3) LIMITED, Plaintiffs, v. GILEAD SCIENCES, INC., Defendant.	Civil Action No. **JURY TRIAL DEMANDED**

COMPLAINT

Plaintiffs ViiV Healthcare Company ("ViiV"), Shionogi & Co., Ltd. ("Shionogi"), and ViiV Healthcare UK (No. 3) Limited (collectively "Plaintiffs"), for their Complaint against Defendant Gilead Sciences, Inc. ("Gilead"), hereby allege as follows:

THE PARTIES

1. Plaintiff ViiV is a corporation organized and existing under the laws of the State of Delaware, with its principal place of business at Five Moore Drive, Research Triangle Park, North Carolina 27709.

2. ViiV is a global company that develops innovative solutions for the treatment of people living with HIV/AIDS and was established in 2009 through a partnership between GlaxoSmithKline ("GSK") and Pfizer. In 2012, Shionogi joined the ViiV partnership following a long-term joint development collaboration with GSK.

3. ViiV offers a broad portfolio of antiretroviral medicines and an industry-leading pipeline of potential treatment options. ViiV is equipped to move quickly in response to the needs of the HIV community and has launched industry-leading access initiatives to help deliver on World Health Organization/UNAIDS goals to reach all those who need treatment.

4. Plaintiff Shionogi is a corporation organized and existing under the laws of Japan, with its principal place of business at 1-8, Doshomachi 3-chome, Chuo-ku, Osaka 541-0045, Japan.

5. Shionogi was founded in 1878 as a drug wholesale business in Osaka, Japan. Since that time, Shionogi has strived to supply the best possible medicine to protect the health and well-being of the patients it serves.

6. On information and belief, Defendant Gilead is a corporation organized and existing under the laws of the State of Delaware, with its principal place of business at 333 Lakeside Drive, Foster City, California 94404.

NATURE OF THE ACTION

7. This is a civil action for patent infringement arising under the Patent Laws of the United States, 35 U.S.C. § 1 *et seq*.

JURISDICTION AND VENUE

8. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

9. This Court has personal jurisdiction over Gilead because, among other things, Gilead is a Delaware corporation that, having availed itself of Delaware's corporate laws, is subject to personal jurisdiction in Delaware.

10. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391(b) and (c), and 1400(b), at least because Gilead resides in this District within the meaning of 28 U.S.C. § 1400(b).

TECHNICAL BACKGROUND

11. Human immune deficiency virus ("HIV") is a retrovirus that causes HIV infection. In a series of steps, the HIV virus targets certain white blood cells (CD4+ cells) in the

host human body, uses those cells to replicate the virus, and then kills the human host's CD4+ cells. First, the virus binds to receptors on the surface of a CD4+ cell. Second, the virus and the target cell membrane fuse together, allowing the virus to enter the CD4+ cell. Once inside the CD4+ cell, the virus releases two viral ribonucleic acid ("RNA") strands and three enzymes. The three enzymes are HIV reverse transcriptase, HIV integrase (the main enzyme at issue here), and HIV protease. The virus next uses the reverse transcriptase enzyme to convert viral RNA into viral deoxyribonucleic acid ("DNA"). The viral DNA then enters the host CD4+ cell's nucleus, where the human host's DNA is located. Once inside the CD4+ cell's nucleus, the HIV viral integrase enzyme inserts the viral DNA into the human host's DNA. That integration step occurs in two parts. First, the HIV integrase enzyme removes a dinucleotide from each end of the viral DNA, generating two 3' hydroxyl recessed termini. Second, a transesterification reaction occurs whereby the 3' hydroxyl groups of the viral DNA bond with the phosphodiester backbone of the human host's cellular DNA. This bonding integrates the viral DNA into the human host's immune cell. After the HIV DNA is integrated into host DNA, the CD4+ cell's normal biological processes generate new HIV RNA, as well as HIV structural proteins, with the assistance of the HIV enzyme protease. Protease participates in the processing of the virus' structural proteins, which are the building blocks for more HIV viruses.

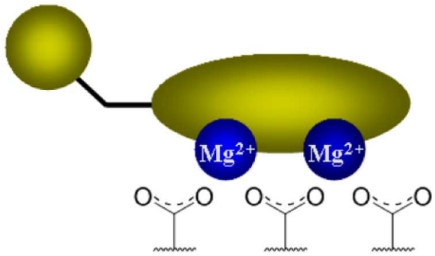
12. CD4+ cells infected with HIV undergo accelerated apoptosis (cell death). As a result, over time, an HIV infection can lead to acquired immune deficiency syndrome ("AIDS"). AIDS is a disease that often results in life-threatening infections and cancers as a result of immune system failure due to the loss of CD4+ cells.

13. Researchers have developed a number of different ways to interfere with the HIV viral lifecycle, and thereby treat HIV infection. Many of those treatments interfere with the

different enzymes and steps in HIV infection and replication. The treatments include the use of reverse transcriptase inhibitors, integrase strand transfer inhibitors, and protease inhibitors. Reverse transcriptase inhibitors are compounds that prevent the conversion of viral RNA into viral DNA, a critical step in HIV replication. Integrase strand transfer inhibitors ("INSTIs"), including those disclosed in the '385 patent, are compounds that prevent the integrase enzyme from causing viral DNA from being incorporated into host DNA in the CD4+ cell. Protease inhibitors are compounds that prevent protease from breaking up large HIV structural proteins into smaller structural proteins, thereby preventing assembly of new, infectious HIV viruses. Combination therapy using the above classes of inhibitors, called highly active antiretroviral therapy ("HAART"), has been generally successful in treating HIV/AIDS.

THE GLAXOSMITHKLINE AND SHIONOGI COLLABORATION

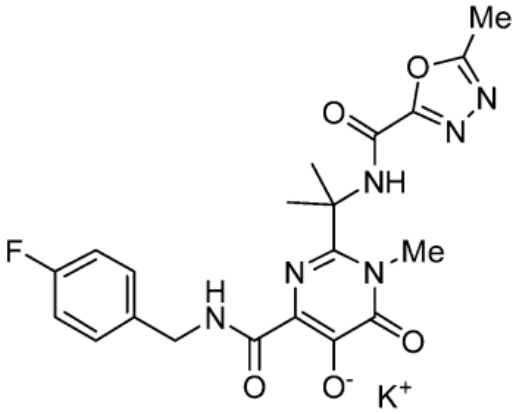
14. In 2001, teams of scientists at GSK and Shionogi began collaborating on a project to develop new and improved INSTIs. The combined team, which at times had more than 24 full time scientists, was interested in expanding the scope of two-metal binding pharmacophore concept (*e.g.*, as graphically depicted below) to find new chemical scaffolds with improved properties, such as improved pharmacokinetic (*i.e.*, the compound's metabolism in the human body) and resistance (*i.e.*, the compound's ability to remain effective against mutant viruses) profiles.



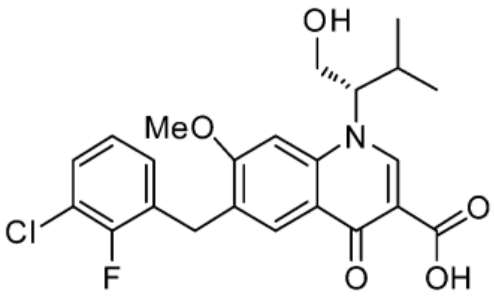
Pictorial Representation of the Two-Metal Binding Pharmacophore

In 2001, the structure of the HIV integrase enzyme was not fully known. However, scientists knew that the HIV integrase enzyme used two-metal binding pharmacokinetics. The basic concept of two-metal binding pharmacokinetics involves a drug molecule (represented in yellow above) binding the two metal atoms in integrase (Mg^{2+}, represented in blue above), essentially blocking the HIV virus from binding the same two metal atoms in integrase, and thus preventing the HIV viral DNA from being integrated into human cellular DNA.

15. When the GSK and Shionogi INSTI project began, several first generation INSTI clinical candidates existed. One compound, raltegravir was first marketed by Merck as ISENTRESS in 2007. Merck scientists received the Heroes of Chemistry Award from the American Chemical Society in 2013 for developing ISENTRESS as the first approved integrase inhibitor for use in HIV infected patients. The other compound, elvitegravir was first marketed in 2012 by Gilead as STRIBILD, a four-drug, one-pill, once-a-day treatment. In 2014, elvitegravir was also marketed by Gilead as VITEKTA, a one-pill, once-a-day treatment to be used in combination with an HIV protease inhibitor coadministered with ritonavir and with other antiretroviral drug(s); however, Gilead voluntarily withdrew VITEKTA from the global market between 2016 and 2017.



Merck's Raltegravir (RAL)



Gilead's Elvitegravir (EVG)

16. The first generation INSTIs had significant shortcomings. The drugs had burdensome administration regimens and poor activity against mutant forms of the HIV virus. GSK and Shionogi sought to avoid those characteristics in developing a new generation of INSTI compounds. For example, although raltegravir was the preferred INSTI in many HAART regimens for treatment of both naïve (i.e., previously non-treated patients) and experienced patients, patients had to take raltegravir twice daily. Further, raltegravir was not active against common mutants, and had demonstrated lack of activity for certain mutants (N155H, Q148H/K/R, and Y143C/R[1]). Similarly, patients had to take elvitegravir with a separate pharmacokinetic booster drug. The booster could interfere with dosing of other medications. Raltegravir was not active against common mutations and had significant cross resistance mutations with elvitegravir. This meant that a patient who became resistant to elvitegravir could not switch to raltegravir.

[1] These are abbreviations used by those in the field to identify HIV mutations impacting specific positions in the amino acid sequence of the integrase enzyme.

17. Given those undesirable characteristics, the GSK and Shionogi team was interested in developing novel INSTIs that could be taken once daily, would not require a booster, and would retain efficacy against HIV mutants. With those goals in mind, GSK and Shionogi began pursuing medicinal chemistry efforts to develop a better INSTI molecule.

18. The team worked collaboratively to develop various novel chemical scaffolds, experiment with various substituents, synthesize the new compounds, and test performance of the compounds in inventive proprietary assays.

19. Through this collaborative process, the team was able to identify a novel structural scaffold for chemical compounds that inhibit HIV integrase.

20. The novel structural scaffold had advantageous characteristics, including a rigid planar three-ring metal-chelating region with an oxygen triad and no bulky side chain, to facilitate binding and protect critical moieties, the third-ring ("ring A") having an oxygen for improved binding strength, a flexible extended linker region that allows deeper entry by the hydrophobic region into the integrase binding pocket vacated by the viral DNA base, and the ability to conform in response to structural changes in the active site.

21. The novel structural scaffold presented a foundation for developing a new generation of INSTIs including dolutegravir. Unlike raltegravir and elvitegravir, dolutegravir remains active against a wide variety of mutant strains of the HIV virus, and can be administered once daily without a pharmacokinetic booster. Dr. Brian Johns of GSK and Dr. Takashi Kawasuji of Shionogi jointly received the Heroes of Chemistry Award from the American Chemical Society in 2016 for their discovery of dolutegravir.

22. The GSK and Shionogi team patented their invention in U.S. Patent No. 8,129,385 ("the '385 patent") .

THE ’385 PATENT

23. The inventions of the ’385 patent originated from the pioneering work performed by GSK and Shionogi in the field of HIV integrase strand transfer inhibitors. The ’385 patent, entitled “Substituted 5-hydroxy-3,4,6,9,9a, 10-hexanhydro-2h-1-oxa04a,8a-diaza-anthracene-6,10-dioness,” was duly and legally issued by the United States Patent and Trademark Office on March 6, 2012. A copy of the ’385 patent is attached hereto as Exhibit A.

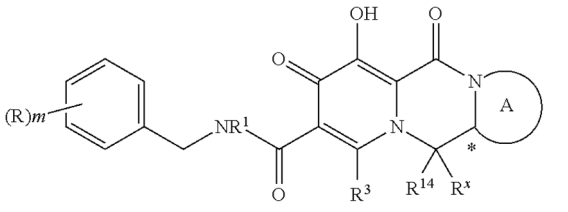
24. Dr. Brian Johns of GSK and Dr. Takashi Kawasuji, Dr. Teruhiko Taishi, and Dr. Yoshiyuki Taoda, of Shionogi, are the listed inventors on the ’385 patent. The ’385 patent claims priority to two Japanese patent applications, Application No. 2005-131161, with a priority date of April 28, 2005 and Application No. 2005-312076, with a priority date of October 27, 2005 and a Patent Cooperation Treaty (“PCT”) application, International Application No. PCT/US2006/016604, filed on April 28, 2006. On November 2, 2006, the PCT application published as Publication No. WO2006/116764. On July 28, 2009, the inventors filed U.S. Application No. 11/919,386, entering the U.S. national stage, claiming priority to the PCT application. On December 24, 2009, the U.S. application published as U.S. Publication No. 2009/0318421. On March 6, 2012 the U.S. application issued as U.S. Patent No. 8,129,385.

25. The ’385 patent discloses, among other things, a novel structural scaffold for chemical compounds that inhibit HIV integrase and are therefore useful as anti-HIV agents.

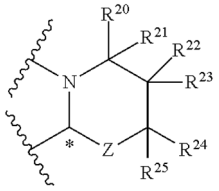
26. For example, claim 1 of the ’385 patent recites:

A compound of the formula:

(I-1-1)



wherein, ring A is



Z = O;

R^{20}, R^{21}, R^{22}, R^{23}, R^{24} and R^{25} are independently hydrogen, C_1-C_8alkyl, C_6-C_{14}arylC_1-C_8alkyl, C_6-C_{14}aryl, or alkoxy;

the stereochemistry of an asymmetric carbon represented by * shows R- or S-configuration, or a mixture thereof;

R^X is hydrogen;

R^{14} is hydrogen or lower alkyl which is optionally substituted with 1 to 4 substituents selected from the group consisting of hydroxy, carboxy, halogen, halo lower alkyl, halo lower alkoxy, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkenyl, lower alkoxy, lower alkenyloxy, lower alkoxycarbonyl, nitro, nitroso, amino, alkylamino, acylamino, aralkylamino, aryl, aralkyl, cyano, isocyano, isocyanate, thiocyanate, isothiocyanate, mercapto, alkylthio, alkylsulfonyl, alkylsulfonylamino, carbamoyl, alkylcarbamoyl, sulfamoyl, acyl, formyloxy, haloformyl, oral, thioformyl, thiocarboxy, dithiocarboxy, thiocarbamoyl, sulfino, sulfo, sulfoamino, hydrazino, azido, ureido, guanidino, phthalimide, oxo, phosphoric acid, lower alkyl which is substituted with phosphoric acid and may be intervened with a heteroatom, aryl substituted with phosphoric acid, aralkyl substituted with phosphoric acid and hydroxy lower alkyl;

R^3 is hydrogen;

R^1 is hydrogen or lower alkyl;

R is halogen;

and

m is 1, 2 or 3;

or a pharmaceutically acceptable salt thereof.

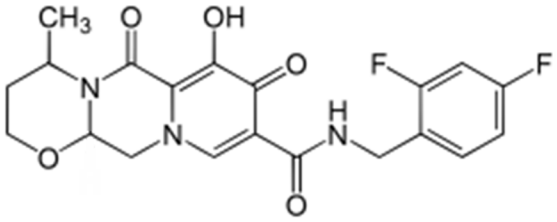
27. Claim 2 of the ’385 patent recites:

A compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R^X is hydrogen; R^{14} is hydrogen; R^3 is hydrogen; m is 1, 2 or 3 and R is halogen.

28. Claim 6 of the ’385 patent recites:

> A compound selected from the group consisting of (4R,9aS)-5-Hydroxy-4-methyl-6,10-dioxo-3,4,6,9,9a,10-hexahydro-2H-1-oxa-4-a,8a-diaza-anthracene-7-carboxylic acid 2,4-difluoro-benzylamide; an enantiomer thereof; diastereomer thereof; mixtures of enantiomers thereof; mixtures of diastereomers thereof; mixtures of enantiomers and diastereomers thereof; or a pharmaceutically acceptable salt thereof.

29. For example, while there are 4 distinct compounds recited in claim 6, the general compound with undefined stereochemistry is represented below:



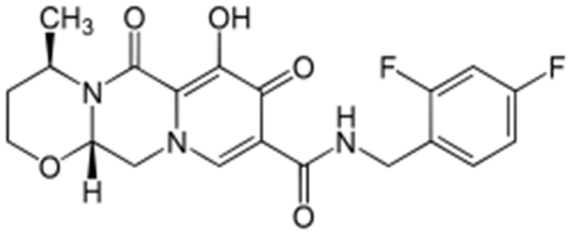
30. Plaintiffs are the exclusive owners of all rights, title, and interest in the ’385 patent, and have the right to bring this suit to recover damages for any current or past infringement of the ’385 patent.

DOLUTEGRAVIR (TIVICAY®)

31. Dolutegravir (“DTG”), brand name Tivicay® (formerly S/GSK1349572), was first synthesized by Shionogi, as part of the GSK and Shionogi collaboration, in February 2006 after years of work.

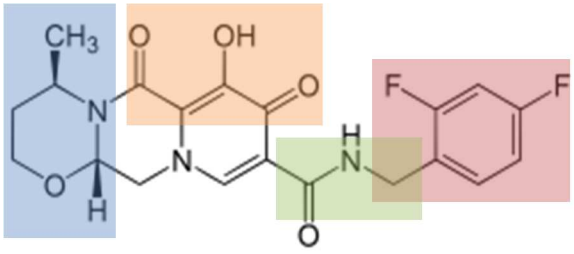
32. DTG has the following chemical formula: $C_{20}H_{19}F_2N_3O_5$.

33. DTG has the following chemical structure:



Dolutegravir (DTG)

34. DTG uses the novel structural scaffold developed by the GSK and Shionogi team and claimed in the '385 patent. DTG has a rigid planar three-ring metal-chelating region with an oxygen triad (represented in orange below) and no bulky side chain, the ring A (represented in blue below) has an oxygen for improved binding strength, the flexible extended linker region (represented in green below) allows deeper entry by the hydrophobic region (represented in red below) into the integrase binding pocket vacated by the viral DNA base, and the ability to conform in response to structural changes in the active site.



Dolutegravir (DTG) Exemplary Scaffold Regions

35. DTG was specifically disclosed as Example Y-3 in the PCT application filed on April 28, 2006. The PCT application published to the public on November 2, 2006. The PCT application is disclosed on the face of four U.S. patents assigned to Gilead.

36. DTG meets the limitations of at least claims 1, 2, and 6 of the '385 patent.

37. DTG is indicated for use in combination with other antiretroviral medicines for the treatment of HIV infection. DTG is offered in 10, 25, and 50mg tablets (Tivicay®). In treatment naïve patients, and in treatment-experienced patients who have not previously taken an integrase inhibitor, DTG is taken in most cases once a day and without a pharmacokinetic booster. DTG is available in over 100 countries across North America, Europe, Asia, Africa, and Latin America.

38. DTG has been extensively studied in multiple Phase III clinical trials involving thousands of adults living with the HIV virus.

39. The clinical data show that DTG is a vast improvement over raltegravir and elvitegravir such that DTG is a "Second Generation" INSTI.

40. For instance, ViiV's "Spring-2" Phase III clinical trial, which started in October 2010, reached primary completion in February 2012, and was fully completed in December 2016, evaluated once-daily DTG versus twice-daily raltegravir in 822 HIV-infected, treatment-naïve patients, in each case in combination with a fixed-dose dual-NRTI treatment. At week 48, the proportion of study participants who were virologically suppressed (HIV-1 RNA <50 c/mL) was 88% for the regimen containing DTG and 86% for the regimen containing raltegravir, meeting the 10% non-inferiority criteria.

41. Further, ViiV's "Single" Phase III clinical trial evaluated once-daily DTG plus abacavir/lamivudine versus the single tablet regimen Atripla in 833 HIV-infected, treatment-naïve patients. At 48 weeks, the proportion of study participants who were virologically suppressed (HIV-1 RNA <50 c/mL) was 88% for the DTG regimen and 81% for Atripla. That difference was statistically significant. Overall, 2% of subjects on the DTG-based regimen discontinued due to adverse events versus 10% of those receiving the Atripla regimen.

42. Moreover, ViiV's "Sailing" Phase III clinical trial evaluated once-daily DTG versus twice-daily raltegravir in 719 patients with the HIV virus who were failing on current therapy, but had not been treated with an integrase inhibitor, in combination with an investigator-selected background regimen consisting of up to two agents, including at least one fully active agent. At week 24, 79% of patients on the regimen containing DTG were virologically

suppressed (HIV-1 RNA <50 c/mL) versus 70% of patients on the regimen containing raltegravir. That difference was statistically significant.

43. Finally, ViiV's "Viking-3" Phase III clinical trial evaluated twice-daily DTG in 183 HIV-infected adults currently on medication whose HIV virus was resistant to multiple classes of HIV medicines, including INSTIs, such as raltegravir and/or elvitegravir. In the study, mean HIV RNA levels declined by 1.4 log10 c/mL after seven days of treatment with the addition of DTG to their background regimen. The proportion of study participants who were subsequently virologically suppressed (HIV-1 RNA <50 c/mL) with the addition of DTG to their background regimen was 63% at week 24.

44. On December 17, 2012, ViiV announced the submission of regulatory applications in the European Union, United States, and Canada for the investigational integrase inhibitor DTG for the treatment of HIV infection in adults and adolescents. On August 12, 2013, DTG was approved by the U.S. Food and Drug Administration ("FDA") to treat HIV-1 infection. In October 2013, DTG was approved by the Canadian regulatory authority in Health Canada. On January 16, 2014, DTG was approved by the European Commission. In April 2014, DTG was approved by the Japanese Pharmaceuticals and Medical Devices Agency. On June 10, 2016, the FDA approved reduction in the weight limit of patients who can take DTG from 40kg to 30kg, meaning children and adolescents are now eligible to receive that treatment.

45. Since approval, DTG has become an important treatment option and is the leading prescribed core agent for HIV treatment. Thousands of patients have been treated with DTG and no known patient has ever developed a resistance.

GILEAD'S AWARENESS OF DTG AND VIIV'S PATENT

46. ViiV disclosed DTG's chemical structure to the public on February 17, 2010 at the 17th Conference on Retroviruses and Opportunistic Infections (the "CROI conference") in San Francisco, California. The CROI conference is an annual conference that brings together top scientists from around the world to share with each other, with clinicians, and with policy makers the latest studies, important developments, and best methods in the ongoing battle against HIV/AIDs. The registered attendees often number 4000 from more than 87 countries. Gilead was represented at the CROI conference. In fact, on February 17, 2010, Gilead's representatives presented data at the CROI conference regarding Gilead's investigational fixed-dose single-tablet "Quad" regimen of elvitegravir, GS 9350 (cobicistat) and Truvada® (emtricitabine and tenofovir disoproxil fumarate) for the treatment of HIV infection.

47. At least by October 13, 2010, the Annual Report in Medicinal Chemistry Volume 45 was available online. Dr. Brian Johns authored Part V, Chapter 16 of Volume 45 titled "HIV-1 Integrase Strand Transfer Inhibitors", which was one of the earliest publications containing DTG's structure. *See* Johns, Brian A. Chapter 16 - HIV-1 Integrase Strand Transfer Inhibitors, In: John E. Macor (Ed.), *Annual Reports in Medicinal Chemistry*, Academic Press, 2010, Volume 45, 262-276. One of the Section Editors for Volume 45 was the Vice President of medicinal chemistry at Gilead, Dr. Manoj Desai. Dr. Desai's research includes antiviral drugs and he is a co-inventor of a patent covering cobicistat (U.S. Patent No. 8,148,374), which is a booster drug approved for use in the treatment of HIV, including in Gilead's "Quad" regimen.

48. On June 17, 2010, ViiV's PCT application PCT/US2009/006422, which was filed on December 8, 2009, was published as WO2010/068253 (the "'253 publication"). Claim 1 of

the ’253 publication discloses a process for the preparation of a pyridine compound of formula (AA). Formula (AA) is DTG.

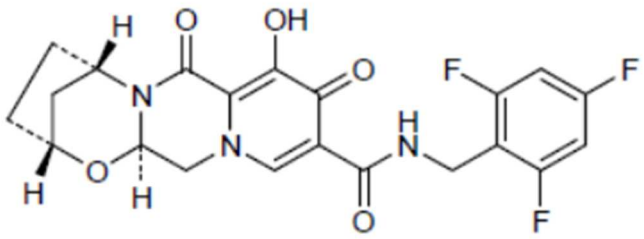
49. On July 1, 2010, a patent review was published in Future Medicinal Chemistry entitled *Authentic HIV-1 Integrase Inhibitors*. The review was performed by parties unrelated to GSK or Shionogi. In the patent review, the authors identified the structure of DTG (S/GSK1349572). *See* Liao, Chenzhong, *et al.*, Future Medicinal Chemistry, July 1, 2010; 2(7): 1107-1122.

50. On April 25, 2012, Gilead scientists published an article in the Journal of Biological Chemistry, entitled *New Class of HIV-1 Integrase (IN) Inhibitors with a Dual Mode of Action*. The Gilead article discusses dolutegravir, among other INSTIs. *See* Tsiang, Manuel, *et al.*, J. Biol. Chem., June 15, 2012; 287(25): 21189-21203.

GILEAD’S BICTEGRAVIR

51. Bictegravir (“BIC”) (formerly GS-9883) was developed and will be marketed and sold by Gilead. BIC has the following chemical formula: $C_{21}H_{18}F_3N_3O_5$.

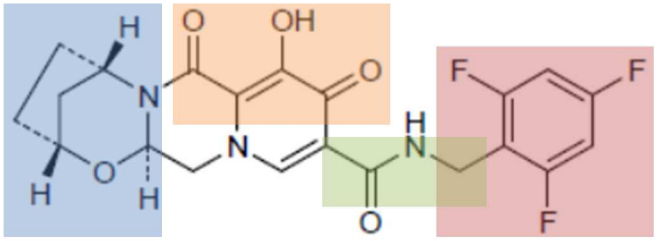
52. BIC has the following chemical structure:



Bictegravir (BIC)

53. BIC includes the novel structural scaffold developed by the GSK and Shionogi team and claimed in ViiV’s ’385 patent. BIC has a rigid planar three-ring metal-chelating region with an oxygen triad (represented in orange below) and no bulky side chain, the ring A

(represented in blue below) has an oxygen for improved binding strength, the flexible extended linker region (represented in green below) allows deeper entry by the hydrophobic region (represented in red below) into the integrase binding pocket vacated by the viral DNA base, and the ability to conform in response to structural changes in the active site.



Bictegravir (BIC) Exemplary Scaffold Regions

54. BIC is an INSTI for treatment of HIV-1.

55. On December 19, 2013, at least three years and ten months after the DTG structure was publicly disclosed, and almost two years after the ’385 patent issued, Gilead filed U.S. Patent Application No. 14/133,858 disclosing *inter alia* BIC and claiming priority to provisional U.S. Patent Application Nos.: 61/745,375 filed December 21, 2012; 61/788,397 filed March 15, 2013; and 61/845,803 filed July 12, 2013. On December 22, 2015, U.S. Application No. 14/133,858 issued as U.S. Patent No. 9,216,996 (“the ’996 patent”).

56. On information and belief, Gilead presented posters at the ASM Microbe conference in June 2016 that discussed BIC (formerly GS-9883). According to those posters, BIC demonstrated favorable pharmacokinetics, good tolerability, a good resistance profile, and potent antiviral activity in laboratory and human studies. In their presentation, Gilead identified the blue region above as the “A-ring.”

57. On May 30, 2017, Gilead announced that four Phase III clinical trials, which evaluated a fixed-dose combination of BIC (50mg), emtricitabine (200mg), and tenofovir alafenamide (25mg) ("BIC/FTC/TAF") for the treatment of HIV-1 infection, met their primary objectives of non-inferiority. Three of the four studies were designed to explore the efficacy and safety of regimens containing BIC compared to regimens containing DTG among treatment-naïve patients (Studies 1489 and 1490) and among virologically suppressed patients switching from an existing antiretroviral regimen (Study 1844). The fourth study tested virologically suppressed patients who switched from a regimen of two nucleoside/nucleotide reverse transcriptase inhibitors and a boosted protease inhibitor (Study 1878).

58. On July 24, 2017, Gilead announced detailed 48-week results from two Phase III clinical trials (Studies 1489 and 1490). Study 1489 contained 629 treatment-naïve adults with the HIV virus who randomly received either the BIC/FTC/TAF regimen or the abacavir (600mg), DTG (50mg), and lamivudine (300mg) regimen ("ABC/DTG/3TC"). At week 48, 92.4 percent (n=290/314) of patients taking BIC/FTC/TAF and 93.0 percent (n=293/315) of patients taking ABC/DTG/3TC achieved the primary endpoint of HIV-1 RNA levels less than 50 copies/mL (difference: -0.6 percent, 95 percent CI: -4.8 percent to 3.6 percent, p=0.78). Study 1490 contained 645 treatment-naïve adults with the HIV virus who randomly received either the BIC/FTC/TAF regimen or the DTG, emtricitabine, and tenofovir alafenamide regimen ("DTG+FTC/TAF"). At week 48, 89.4 percent (n=286/320) of patients taking BIC/FTC/TAF and 92.9 percent (n=302/325) of patients taking DTG+FTC/TAF achieved the primary endpoint of HIV-1 RNA levels less than 50 copies/mL (difference: -3.5 percent, 95 percent CI: -7.9 percent to 1.0 percent, p=0.12). No patient involved developed a resistance to any of the study drugs.

59. The results of Gilead's Phase III clinical trials indicate no meaningful clinical difference between BIC and DTG.

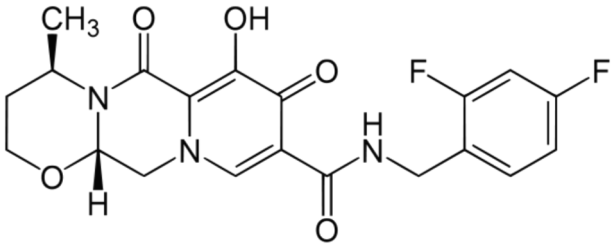
THE SIMILARITIES BETWEEN BIC AND DTG SUGGEST GILEAD COPIED DTG

60. On information and belief, Gilead first synthesized BIC after the DTG chemical structure was publicly disclosed (in February 2010) and with knowledge of the '385 patent.

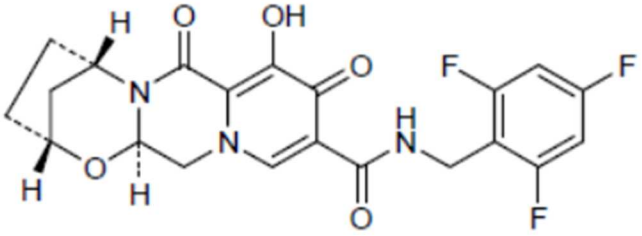
61. On information and belief, Gilead relied on the DTG work performed by GSK and Shionogi in developing BIC.

62. BIC has the same molecular scaffold as DTG and claimed in the '385 patent.

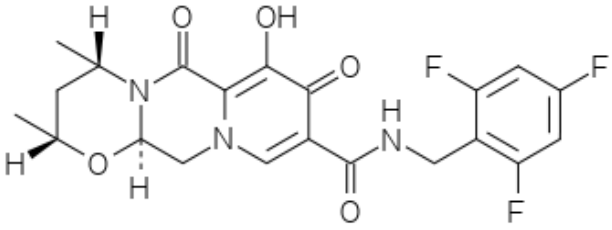
63. BIC is not substantially structurally different from DTG. In particular, BIC's "bridged" ring A does not make BIC substantially different from DTG or the other compounds claimed in the '385 patent.



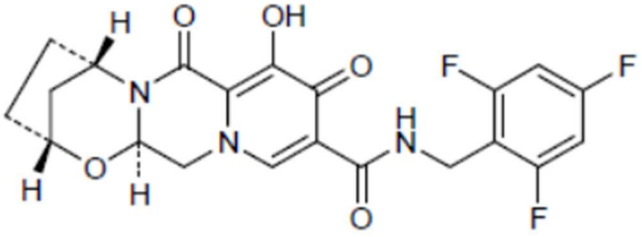
Dolutegravir (DTG)



Bictegravir (BIC)

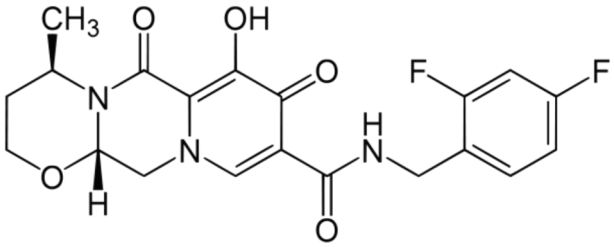


Exemplary Compound Disclosed and Claimed in the '385 Patent

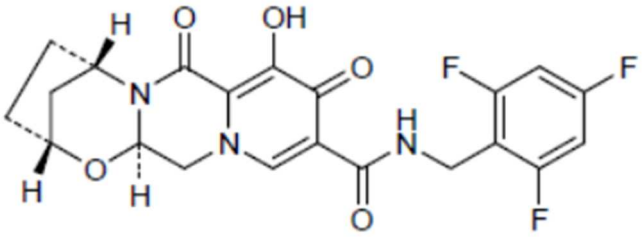


Bictegravir (BIC)

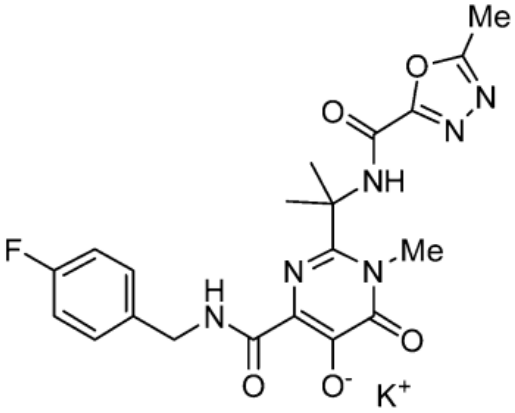
64. The structural similarities between BIC and DTG, or other compounds claimed in the ’385 patent, are far greater than the structural similarities of BIC to any of the first generation INSTIs, such as raltegravir or elvitegravir.



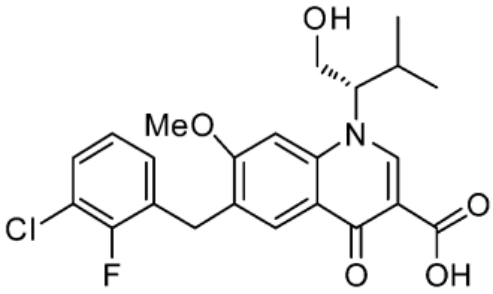
Dolutegravir (DTG)



Bictegravir (BIC)



Raltegravir (RAL)



Elvitegravir (EVG)

65. BIC can be synthesized using the process disclosed in the ’385 patent.

66. The ’385 patent is listed in the Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book) for Tivicay® (dolutegravir sodium tablets in 10, 25, and 50 mg bases) and Triumeq® (abacavir sulfate (600mg), dolutegravir sodium (50mg), and lamivudine (300mg) tablets), and Juluca® (dolutegravir sodium (50mg) and rilpivirine hydrochloride (25mg) tablets).

67. On June 12, 2017, Gilead filed a New Drug Application ("NDA") to the FDA with a Priority Review voucher for an investigational, fixed-dose combination of BIC/FTC/TAF for the treatment of HIV-1 infection.

68. On July 13, 2017, Gilead announced that a Marketing Authorization Application ("MAA") for BIC/FTC/TAF was validated by the European Medicines Agency ("EMA") and was under evaluation.

69. On July 24, 2017, Gilead announced 48-week results from two Phase III clinical trials (Studies 1489 and 1490) indicating that the BIC/FTC/TAF regimen was statistically non-inferior to regimens containing DTG in combination with a dual-NRTI backbone.

70. On August 10, 2017, Gilead announced that the FDA granted priority review for its NDA and the FDA set a target action date under the Prescription Drug User Free Act of February 12, 2018.

71. On information and belief, Gilead was aware of and reviewed the '385 patent prior to seeking FDA approval.

72. On February 7, 2018, Gilead obtained FDA approval to market and sell certain pharmaceutical products containing BIC in the United States for the treatment of HIV-1 infection.

73. On information and belief, Gilead began making, using, marketing, offering to sell, selling, and importing BIC in a combination product for the treatment of HIV-1 upon (or before) receiving FDA approval.

74. Plaintiffs have not authorized or licensed Gilead to use any of the inventions claimed in the '385 patent.

COUNT I

Infringement Of The '385 Patent

75. Paragraphs 1 through 74 are incorporated by reference as if fully stated herein.

76. The '385 patent is valid and enforceable.

77. On information and belief, Gilead has infringed, and continues to infringe, at least claims 2 and 6 of the '385 patent under 35 U.S.C. § 271(a) by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, products covered by those claims, including for example, by making, using, selling, offering for sale, and/or importing pharmaceutical products containing BIC, such as Biktarvy®.

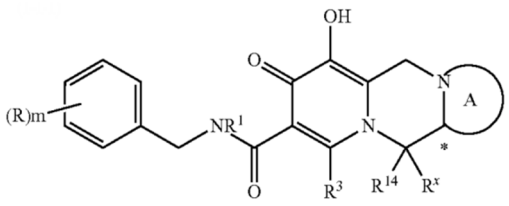
78. On information and belief, third parties, including Gilead's customers, have infringed, and continue to infringe, at least claims 2 and 6 of the '385 patent under 35 U.S.C. § 271(a) by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, BIC/FTC/TAF supplied by Gilead.

79. Gilead has induced infringement, and continues to induce infringement, of at least claims 2 and 6 of the '385 patent under 35 U.S.C. § 271(b). Gilead actively, knowingly, and intentionally induced, and continues to actively, knowingly, and intentionally induce, infringement of the '385 patent by selling or otherwise supplying BIC/FTC/TAF; with the knowledge and intent that third parties will use, sell, and/or offer for sale in the United States, and/or import into the United States, BIC/FTC/TAF supplied by Gilead to infringe the '385 patent; and with the knowledge and intent to encourage and facilitate the infringement through the dissemination of BIC/FTC/TAF and/or the creation and dissemination of promotional and marketing materials, supporting materials, instructions, product manuals, and/or technical information related to BIC/FTC/TAF.

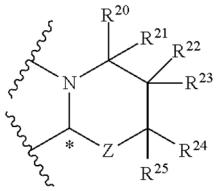
80. On information and belief, Gilead has had knowledge of and notice of the '385 patent, and that BIC would infringe the '385 patent, since at least May 2, 2015, through submission of an Information Disclosure Statement to the United States Patent and Trademark Office identifying the '385 patent during the prosecution of U.S. Patent Application No. 14/133,858.

81. BIC is a compound of formula I-1-1 (depicted below) wherein ring A (depicted below) meets the following criteria: Z is oxygen; at least four of R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, and R^{25} are independently hydrogen or C_1-C_2 alkyl; the stereochemistry of the asymmetric carbon represented by * shows an R-configuration, or a mixture of S- and R-configurations; R^x is hydrogen; R^{14} is hydrogen; R^3 is hydrogen; R^1 is hydrogen; R is halogen; and m is 3.

Formula I-1-1



Ring A



Z = O;

82. Any differences between ring A in the compounds described in claim 2 and the corresponding structure of BIC are insubstantial. As a first non-limiting example, Gilead's reported clinical data for BIC show insubstantial differences from the clinical data reported by ViiV for DTG, an embodiment of *e.g.*, claim 2. As a second non-limiting example, the chemical

and spatial interaction of the HIV integrase protein with the ring A of BIC is insubstantially different from the interaction with the ring A in claim 2. As a third non-limiting example, modeling and simulation of the interaction between HIV integrase and BIC or embodiments of claim 2 show that the spatial profile of and space occupied by the ring A of BIC, on the one hand, is insubstantially different from the spatial profile of and space occupied by the ring A in claim 2, on the other hand. As a fourth non-limiting example, the resistance profile for clinically observed mutations of BIC is insubstantially different from that of DTG, an embodiment of *e.g.*, claim 2, with respect to mutations that implicate interactions between the ring A of BIC and DTG and HIV integrase, such as Q148H/G140S.

83. Moreover, the ring A of BIC performs substantially the same function in substantially the same way with substantially the same result as the ring A as described in claim 2. As a first non-limiting example, the ring A in claim 2 and its equivalent structure in BIC perform substantially the same function (*e.g.*, of structurally and stereochemically stabilizing the adjacent reactive regions of the compound, including the oxygen atom in ring A), in substantially the same way (*e.g.*, by sterically and physically "locking" the conformation of adjacent regions in the compound, without distorting the overall molecular shape in a way that interferes with integrase pocket binding), to achieve substantially the same result (*e.g.*, structurally stabilizing the compound in a configuration that permits deep binding in the integrase pocket, without requiring interaction with amino acids that can interfere with binding and/or are subject to mutation).

84. Any differences between the compounds recited in claim 6 and BIC are insubstantial. As a first non-limiting example, Gilead's reported clinical data for BIC show insubstantial differences from the clinical data reported by ViiV for DTG, an embodiment of

e.g., claim 6. As a second non-limiting example, the chemical and spatial interaction of the HIV integrase protein with the ring A of BIC is insubstantially different from the interaction with the ring A in claim 6. As a third non-limiting example, modeling and simulation of the interaction between HIV integrase and BIC or embodiments of claim 6 show that the spatial profile of and space occupied by the ring A of BIC, on the one hand, is insubstantially different from the special profile of and space occupied by the ring A in claim 6, on the other hand. As a fourth non-limiting example, the resistance profile for clinically observed mutations of BIC is insubstantially different from that of DTG, an embodiment of *e.g.*, claim 6 with respect to mutations that implicate interactions between the ring A of BIC and DTG and HIV integrase, such as Q148H/G140S.

85. The compounds recited in claim 6 perform substantially the same function in substantially the same way with substantially the same result as BIC. As a first non-limiting example, the ring A in claim 6 and its equivalent structure in BIC perform substantially the same function (*e.g.*, of structurally and stereochemically stabilizing the adjacent reactive regions of the compound, including the oxygen atom in ring A), in substantially the same way (*e.g.*, by sterically and physically "locking" the conformation of adjacent regions in the compound, without distorting the overall molecular shape in a way that interferes with integrase pocket binding), to achieve substantially the same result (*e.g.*, structurally stabilizing the compound in a configuration that permits deep binding in the integrase pocket, without requiring interaction with amino acids that can interfere with binding and/or are subject to mutation). As a second non-limiting example, the difluoro benzyl ring in claim 6 and the equivalent trifluoro benzyl ring in BIC perform substantially the same function (*e.g.*, of deeply entering the integrase pocket vacated by displaced viral DNA base), in substantially the same way (*e.g.*, through the extended

flexible linker region allowing the molecule to adopt favorable conformations), to achieve substantially the same result (*e.g.*, favorable interactions within the pocket leading to deeper position and improved integrase strand transfer inhibition over first generation INSTIs, such as raltegravir and elvitegravir). As a third non-limiting example, the compounds recited in claim 6 and BIC perform substantially the same function (*e.g.*, of inhibiting the HIV virus from integrating into human cellular DNA), in substantially the same way (*e.g.*, by blocking HIV from reaching the active site without interfering with deep integrase pocket binding), to achieve substantially the same result (*e.g.*, deep binding in the integrase pocket, without requiring interaction with amino acids that can interfere with binding and/or are subject to mutation, and improved integrase strand transfer inhibition over first generation INSTIs).

86. Gilead's infringement of the '385 patent was, and continues to be willful: Gilead's infringement was deliberate, malicious, consciously wrongful, egregious, and/or in bad faith, rendering this case exceptional and permitting Plaintiffs to seek enhanced damages under 35 U.S.C. § 284 and attorneys' fees and costs incurred in prosecuting this action under 35 U.S.C. § 285. On information and belief, Gilead had, and continues to have, knowledge of the '385 patent. Gilead's infringement of the '385 patent was, and continues to be with full and complete knowledge of the '385 patent and its applicability to BIC without any attempt to take a license under the '385 patent and without a good faith belief that the '385 patent is invalid or not infringed.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs pray for judgment as follows:

A. That Gilead has infringed the '385 patent;

B. That Gilead's infringement of the '385 patent has been willful;

C. That Plaintiffs be awarded damages adequate to compensate them for Gilead's infringement of the '385 patent, such damages to be determined by a jury and, if necessary to adequately compensate Plaintiffs for the infringement, an accounting, and that such damages be trebled and awarded to Plaintiffs with pre-judgment and post-judgment interest;

D. That this case by declared an exceptional case within the meaning of 35 U.S.C. § 285 and that Plaintiffs be awarded the attorney fees, costs, and expenses incurred in connection with this action; and

E. That Plaintiffs be awarded such other and further relief as this Court deems just and proper.

DEMAND FOR JURY TRIAL

Plaintiffs hereby demand a trial by jury on all issues so triable.

Dated: February 7, 2018

MCCARTER & ENGLISH, LLP

/s/ Daniel M. Silver

Michael P. Kelly (#2295)
Daniel M. Silver (#4758)
Renaissance Centre
405 N. King Street, 8th Floor
Wilmington, Delaware 19801
(302) 984-6300
mkelly@mccarter.om
dsilver@mccarter.com

Attorneys for Plaintiffs, ViiV Healthcare Company, Shionogi & Co., Ltd., and ViiV Healthcare UK (No. 3) Limited

OF COUNSEL:

John M. Desmarais
Michael P. Stadnick
Justin P.D. Wilcox
Lindsey E. Miller
Michael D. Jenks
Kyle G. Petrie
DESMARAIS LLP
230 Park Avenue
New York, New York 10169
(212) 351-3400
jdesmarais@desmaraisllp.com
mstadnick@desmaraisllp.com
jwilcox@desmaraisllp.com
lmiller@desmaraisllp.com
mjenks@desmaraisllp.com
kpetrie@desmaraisllp.com