PATENT COOPERATION TREATY

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THIRD PARTY OBSERVATION

(PCT Administrative Instructions Part 8)

Applicant's or agent's file reference 35648-0292WO1	
International application number PCT/US2024/031478	International filing date (day/month/year) 29 May 2024 (29/05/2024)
Applicant GILEAD SCIENCES, INC.	

Third party observation submitted by Anonymous	Observation submitted on behalf of
Date of submission(day/month/year) 30 Sep 2025 (30/09/2025)	Language of observation English

Basis and contents of observation

1. The observation is made on the basis of the claims in the international application as filed.
2. The observation comprises:
   References to documents: 5
   Uploaded copies of documents: 5
3. Further explanations:
   Uploaded copies of documents: 1

Citation # 1 (Patent/utility model) (# uploaded documents: 0):

Country code:	Publication number:	Document kind code:
WO	2020/028272	A1

Patent Applicant/Patent Owner:	Title of invention:
Gilead Sciences, Inc.	Anti-HIV compounds

Link to document:
https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2020028272

Publication Date:	Filing Date:	Priority Date:
06 Feb 2020 (06/02/2020)	29 Sep 2019 (29/09/2019)	30 Sep 2018 (30/09/2018)

Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:

Most relevant passages or drawings:	Relevant to Claims:
p. 44, Claims 1–99	1 to 150

Brief explanation of relevance:

As shown below, WO2020028272 (WO272) is a patent application by Gilead Sciences, Inc. for prodrugs of certain atazanavir analogues, including GS-PI1 now also known as elunonavir. WO272 discloses that the compounds claimed therein may be metabolised in vivo to form therapeutic compounds disclosed in US App. No. 62/455,348 [priority document of WO2018145021 (WO021; attached as Citation 1A hereto)] (p.1). It may be noted that these atazanavir analogues disclosed by WO021 and WO272 are HIV protease inhibitors.

The present Application, WO2024249517 (WO517), claims different types of prodrugs for the same known atazanavir analogues, including elunonavir.

Tables of comparison showing similarity in: (a) the Markush structures and substituents of the parent molecule (i.e., atazanavir analogues); and (b) secondary claims—claimed in WO272 and the present Application, WO517, are added as Tables B and C in the Annexure to the “Additional Comments” filed herewith.

Basically, WO272 discloses and/or claims:

1. Prodrugs of certain atazanavir analogues of Formula I, where the OH of the parent molecule (disclosed in WO021) is derivatised to form ester prodrugs—i.e., the acyl, alpha-amino acid, cyclic amino acid and phosphate ester prodrugs (Claims 1–55). [Refer to the “Additional Comments” for a detailed comparison of the Markush structures and the various substituents claimed.]

2. Prodrugs specifically of compound D, i.e., methyl ((5S,8S,9S,14S)-11-(4-(1-(difluoromethyl)-1H-pyrazol-3-yl)- 2,6-difluorobenzyl)-16,16,16-trifluoro-9-hydroxy-15,15-dimethyl-8-(4-((2-(8-(oxetan-3-yl)-3,8-diazabicyclo[3.2.1]octan-3-yl)pyrimidin-5-yl)ethynyl)benzyl)-3,6,13-trioxo-5-(1,1 -trifluoro-2-methylpropan-2-yl)-2-oxa-4,7,11,12-tetraazahexadecan-14-yl)carbamate (Claims 42–55; pp.72–90; Part 1, Part 2: Examples 1–14) [It may be noted that compound D is GS-PI-1 disclosed in WO021]
3. Pharmaceutical composition thereof, with a pharmaceutically acceptable excipient (Claim 56).
4. Such composition further comprising one, two, three or four additional therapeutic agents including tenofovir, abacavir, bictegravir, various capsid inhibitors, etc. (Claims 57–61, 82–85, 94–95).
5. Method of treating or preventing HIV therewith, either by administering it alone or in combination with other additional therapeutic agents (Claims 62–67, 86–89, 96).
6. Such compound or its salt for use in therapy, either alone or in combination with other additional therapeutic agents; use of such compound or its salt in the manufacture of a medicament to treat HIV (Claims 68–78, 90–93, 98–99; p. 44).
7. Biological data for some of the claimed prodrugs of compound D (GS-PI1, now known as elunonavir) (pp.90–94).

Further, WO021 [Citation 1A], the application for the parent atazanavir analogues, claims the analogues as well as discloses prodrugs thereof [Claims 1–57; p. 14 of WO021]. WO021 also claims pharmaceutical composition of such atazanavir analogues, alone and in combination with other anti-HIV agents, as well as methods for treating and preventing HIV therewith and use thereof [Claims 58–101 of WO021]. WO021 specifically discloses GS-PI1, now known as elunonavir and referred to as Compound D in WO272 [Citation 1; Example 58, pp.185–186]. WO021 also discloses the biological activity of some of the claimed atazanavir analogues [Part 4, pp.339–359].

The present Application, WO517, claims protease inhibitors of formulae I-XI (it may be noted that the compounds of WO517 represent carboxylate ester prodrugs of elunonavir), wherein the -OH group is linked to the trimethyl lock (TML)- containing promoieties, wherein the -OH and methyl substitution on the phenyl group is further derivatized to a phosphonooxy group and a substituted amide group (particularly amino acid or modified amino acid group, Claim 85), respectively (Claims 1–89). WO517 further claims pharmaceutical composition thereof along with additional therapeutic agents (e.g., lenacapavir), method of treating/preventing HIV therewith, compound for use, use of compound, etc. (Claims 90–150).

However, as is clear from Tables B and C comparing the Markush structures and the secondary claims of WO272 and the present Application, WO517 [refer to Annexure to the “Additional Comments”], the present Application merely claims different types of prodrugs of known atazanavir analogues. The Applicant has employed the known prodrug strategy of TML-containing promoieties [Dillon et al., and Walther et al.; Citations 3 and 3A, respectively] to known atazanavir analogues.

In light of the above, Claims 1 to 150 of the present Application, WO517, lack inventive step.

Citation # 2(Periodical article) (# uploaded documents:2):

Author:	Title of article:	Title of Periodical:	Publication Date:
Subbaiah, M. A. M., et al.	Design strategies in the prodrugs of HIV-1 protease inhibitors to improve the pharmaceutical properties	European Journal of Medicinal Chemistry	20 Oct 2017 (20/10 /2017)
Issue Number of Periodical:	Publisher of Periodical:		Place of publication:
Volume 139	Editions Scientifiques Elsevier		France

Page range of article within periodical:	ISBN:	ISSN:
865–883		0223-5234

DOI: 10.1016/j.ejmech.2017.07.044

Most relevant passages or drawings:	Relevant to Claims:
Abstract; pp.866–871, 873–874, 876, 878, 881; Figs. 1, 2, 3, 5, 7,12, 14, 21; Table 7	1 to 150

Brief explanation of relevance:

Subbaiah, et al. review rational prodrug design as a path to optimize the delivery of protease inhibitors (PIs) and improve pharmacokinetics (PK) (Abstract; pp.866–867; Fig.1). They set out the ADME limitations of HIV-1 PIs, such as atazanavir (ATV), including poor bioavailability due to poor solubility, modest permeability and extensive first-pass metabolism. These limitations lead to high pill burden and high daily doses (p.867, LHC; Fig.2). They state that phosphate prodrugs and acyl prodrugs have been explored to enhance solubility, whereas amino acid prodrugs have been shown to improve permeability, reduce efflux and mitigate first-pass metabolism (Abstract, p.868, RHC).

Subbaiah, et al. disclose the following:

1. Despite the availability of diverse attachment points on the PIs, prodrug efforts have exclusively utilized the group OH as a handle, particularly the secondary OH of the pharmacophore (p.868, LHC).
2. Prodrug-based approaches proposed in the literature include (p.868, 869; Fig.3):
a) The direct attachment of promoiety to the drugs (direct prodrugs): e.g., fosamprenavir (clinically approved);
b) Drug–linker–promoiety containing prodrugs (spacer containing prodrugs): (note: promoiety can be phosphate group or amino acid);
c) O–N acyl migration prodrugs.
3. Directly linked prodrugs may encounter steric constraints at the point of attachment , which can limit enzyme access to promoieties and interfere with bioactivation; to overcome this problem, linkers are introduced. The linkers may be: (i) those that release parent drug through two steps of successive activation of the pro-moiety and the resulting intermediate (ii) self–immolative linkers (p. 868, RHC).
4. Design of amino acid prodrugs: PI pharmacophore-optional linker-amino acid (p.871; Fig.7).
5. Amino acid prodrugs of PI pose limited safety concerns associated with release of the prodrug moiety and improve solubility (p.869, RHC; 871, LHC; 873 Fig.12).
6. Phosphate prodrugs of PI were designed to reduce pill burden. Direct phosphate prodrugs failed ALP dephosphorylation. Acetal-linked prodrugs improved solubility and projected the promoiety away from the peptidomimetic core, good stability at pH 7.4 (pp.868, 869, RHC; 870; Fig.5).
7. Ester and carbamate-based amino acid prodrugs of PI have been reported. Prodrugs with linker moiety, i.e. PI–linker–amino acid prodrugs showed improved chemical stability, indicating that the linker enhances resistance to hydrolysis (p.874, LHC; Fig.14).
8. A water-soluble promoiety, a self-immolative linker with an ionizable amine, when attached to the peptidomimetic OH, yielded prodrugs with higher solubility and stability (p.876, RHC; Fig.21).
9. The design and synthesis of ester prodrugs of brecanavir that have drug–linker–promoiety design (p.878 ; Fig.22).

In a later publication, Subbaiah, et al. [2020; DOI: 10.1016/j.ejmech.2020.112749; attached as Citation 2A] describe the following:
1. Amino acid-based prodrugs of ATV employs a (carbonyl)oxyalkyl amino acid ester moiety to achieve efficient drug exposure (Abstract; p.2, LHC; p.3, Fig.2).
2. To overcome inefficient bioactivation observed in directly attached prodrugs, a linker-based prodrug strategy was explored that would project the promoiety away from the core structure of ATV, facilitating better recognition by endogenous enzymes and possibly more efficient in vivo biotransformation to the parent molecule (p.4, LHC).
3. Pathway of parent drug generation from prodrug involving a II-step process of enzymatic hydrolysis followed by self-immolation (p.9, RHC; p.10; Fig.8).

The present Application WO2024249517 (WO517) claims, protease inhibitors of formulae I-XI (it may be noted that the compounds of WO517 are carboxylate ester prodrugs of elunonavir), wherein the -OH group is linked to the trimethyl lock (TML) containing promoieties, wherein the -OH and methyl substitution on the phenyl group is further derivatized to a phosphonooxy group and a substituted amide group (particularly amino acid or modified amino acid group, Claim 85), respectively (Claims 1–89). WO517 further claims pharmaceutical composition thereof along with additional therapeutic agents (e.g., lenacapavir), method of treating/preventing HIV for use (Claims 90–150) (it may be noted that WO517 relates to prodrugs of compound disclosed on p.86 of WO517).

However, in light of above, Subbaiah, et al. [Citations 2 and 2A] already describe the identical categories of prodrugs (including carboxylate esters, amino acid ester, Phosphate etc). Further Dillon et al., and Walther et al. [Citations 3 and 3A, respectively] describes the TML prodrug strategy for antiviral prodrugs.

Thus, in light of Subbaiah, et al. [Citations 2 and 2A] read along with Citations 3 and 3A all Claims of WO517 lack inventive step.

Citation # 3(Periodical article) (# uploaded documents:2):

Author:	Title of article:	Title of Periodical:	Publication Date:
Dillon, M. P., et al.	Application of the "Trimethyl lock" to ganciclovir, a pro-prodrug with increased oral bioavailability	Bioorganic & Medicinal Chemistry Letters	23 Jul 1996 (23/07 /1996)

Issue Number of Periodical:	Publisher of Periodical:	Place of publication:
Volume 6, Issue 14	Elsevier Science Ltd	Oxford, Great Britain

Page range of article within periodical:	ISBN:	ISSN:
1653–1656		

DOI: 10.1016/0960-894X(96)00294-6

Most relevant passages or drawings:	Relevant to Claims:
pp.1653-1655	1 to 150

Brief explanation of relevance:

Dillon et al. describes the synthesis of two potential prodrugs of ganciclovir (GCV) based on the “trimethyl lock” (TML) pro-prodrug strategy, wherein the TML containing prodrug (Compound 2; R1 is TML moiety and R2 is acetate (Ac)), showed a 4-fold increase in oral bioavailability over the parent drug in rats (Abstract; p.1653).

They state the following:

1. The “most common prodrugs are usually esters of drugs that already contain carboxyl or hydroxyl moieties since many enzymes are capable of hydrolyzing simple esters” (p.1653);
2. The pro-prodrug (double prodrug) is an extension of the approach of chemically modifying drugs to improve pharmacokinetic properties where, after absorption, an enzymatic step first liberates a prodrug that is then converted to the parent drug by a secondary mechanism (p.1653);
3. Pro-prodrug approach is a viable alternative in cases where enzymatic hydrolysis is slow which results in reduced biological activity, or where hydrolysis is fast and occurs before absorption, which results in no significant increase in biological activity over the parent drug (p.1653);
4. TML utilises intramolecular lactonization to liberate the parent molecule, and derives it name from the substitution of methyl groups at the 4' and 3 positions within the molecule which are positioned such that, once the lock is triggered, intramolecular cyclization occurs at a rate many orders of magnitude faster than in the unsubstituted case (pp.1653-1654);

5. Among the two mono-ester derivatives of GCV, the compound 2 had the hydroxyl trigger to the TML protected by an esterase-labile Ac group, while in compound 3, Ac replaced by a more stable benzyl (Bz) group (p.1654);
6. In rats, the acetate derivative showed 15.6% oral bioavailability, over 4-fold higher than the 3.6% for GCV's, which "results from absorption followed by esterase-activated hydrolysis of the acetate trigger", which "facilitates rapid intramolecular cyclization to liberate the parent drug", and it is "a clear demonstration of the pro-prodrug principle in action"; while the Bz derivative produced no significant plasma levels, suggesting no ester hydrolysis prior to absorption or non-activation of the trigger (pp.1654-1655);

Further, Walther et al. [2017; DOI:10.1016/j.addr.2017.06.013; Citation 3A] discuss the use of "self-immolative linkers" (SILs) in prodrug design [Abstract; p.2]. They state that enzymatic conversion of prodrugs depends critically on the accessibility of the scissile bond to the enzyme [p.21]. They cite the examples of (i) phosphonoxymethylene prodrug of propofol which was bioconverted markedly faster than the sterically hindered phosphate prodrug due to easier enzyme access and (ii) the paclitaxel-TML-phosphate which was successfully converted by alkaline phosphatase, unlike paclitaxel phosphate; these examples illustrate the concept and marketed use of SILs, which are installed between the trigger and the deliverable drug so as "to degrade spontaneously and fast, and produce byproducts with acceptable safety profile" [pp.21–22; Scheme 12]. They identify TML, inspired by intramolecular lactonization, as an already established SIL, and they state that various structures had been synthesized previously to release amine-containing drugs upon removal of the trigger unit, including phosphorylase-triggered release of peptidic cargo and an amine-containing combretastatin analogue [pp.24–25; Scheme 14].

The present Application WO2024249517 (WO517) claims protease inhibitors of formulae I-XI (it may be noted that the compounds of WO517 represent carboxylate ester prodrugs of elunonavir), wherein the -OH group is linked to the TML-containing promoieties, wherein the -OH and methyl substitution on the phenyl group is further derivatized to a phosphonoxy group and a substituted amide group (,respectively (Claims 1–89). WO517 further claims pharmaceutical composition thereof along with additional therapeutic agents (e.g., lenacapavir), method of treating/preventing HIV therewith, use thereof, etc (Claims 90–150).

However, Dillon et al. already discloses the use of a TML as a pro-prodrug strategy, exemplified by the synthesis of TML-containing GCV derivatives, which led to a 4-fold increase in oral bioavailability in rats. Further, Walther et al. [Citation 3A] disclose the use of TML as a self-immolative linker and its mechanism of drug release through intramolecular lactonization. The present Application, WO517, merely applies the already known TML-based prodrug strategy to known protease inhibitors (disclosed in WO2018145021: Citation 1A).

Thus, all claims of WO517 lack inventive step.

Citation # 4 (Patent/utility model) (# uploaded documents: 1):

Country code:	Publication number:	Document kind code:
WO	1999/033483	A1

Patent Applicant/Patent Owner:	Title of invention:
Enzon, Inc.	Trialkyl-lock-facilitated polymeric prodrugs of amino-containing bioactive agents

Link to document:
https://patentscope.wipo.int/search/en/detail.jsf?docId=WO1999033483

Publication Date:	Filing Date:	Priority Date:
08 Jul 1999 (08/07/1999)	29 Dec 1998 (29/12/1998)	30 Dec 1997 (30/12/1997)

Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:

Most relevant passages or drawings:	Relevant to Claims:
Abstract; pp.1–13, 15, 19–22, 26–28, 32–33; Claims 1–16, 18–19, 29, 34	1 to 150

Brief explanation of relevance:

WO1999033483 (WO483) discloses trialkyl-lock-facilitated double prodrugs of formula I, for addressing problems of the parent compound related to solubility, circulating half-life of the prodrug, etc (Abstract; pp.1, 3).

WO483 refers to Bundgaard et al., [doi: 10.1016/0169-409X(89)90004-5] disclosing non-polymeric-based prodrugs, and notes that cascade latentiation or “pro-prodrugs”, wherein the hydrolytic reaction sequence involves a first step which is usually an enzymatic cleavage followed by a non-enzymatic hydrolysis (p.2).

WO483 discloses and/or claims:

1. Compounds of formula I, wherein (Abstract; Claims 1, 29; pp.4–5, 7–8, 19–22):

1.a) B is a residue of an amine/hydroxyl-containing moiety (pp.26–28)

1.b) L2, bifunctional linking moiety, where G is -C=Y1; Y1 is O; R1 and R4 are alkyl, branched alkyl, ,; p is 0–2 (Claims 1, 3, 11, 18–19; p.10).

1.c) Ar is a multi-substituted aromatic hydrocarbon/heterocyclic group, e.g., phenyl, substituted with R2, R3, R5, R6, selected from alkyl, branched alkyl, substituted alkyl, etc, or selected from carboxyl, acyl, substituted acyl, carboxyalkyl, etc; R2 and R5 are methyl; R3 and R6 is H (Claims 1, 4–8; pp.8–10). [It may be noted that when Y1 is O, p is 1, R1=R4 is CH3, Ar is phenyl substituted with R3=R6=H, R2 and R5 as methyl or derivatives thereof, and the phenolic O is further derivatized, the promoiety is a trimethyl lock (TML) linker]

1.d) Y2 is O (Claims 1, 19).

1.e) L1, a bifunctional linking moiety, is -M-[C(R7)(R8)]n-, wherein M is X (electron withdrawing group, e.g., O, NR12) or Q, (alkyl, cycloalkyl, aralkyl, etc substituted with NH, O, -CH2-C(O)-NH-, etc); R7 and R8 are H, alkyl, branched alkyl, cycloalkyl, substituted/aryl, etc; n is 0 or 1–12 (Claims 1, 2, 12–16; pp.10–12).

1.f) R11 is a water-soluble polymer residue; as an alternative to PEG, polyaminoacids, etc can be used if the same type of activation is employed (Claims 1, 9–10; pp.12, 15).

2. Suitable pharmaceutical compositions of the claimed prodrugs, for oral and/or parenteral administration; method of treatment therewith (Claim 34; pp.32–33).

WO483 also discloses that the linkage between L1 and C(=Y2) is labile and selected so as to hydrolyze (esterase catalyzed) in vivo at a rate to generate sufficient amount of the “second” prodrug compound within a suitable time after administration, followed by spontaneous independent trialkyl lactonization reaction in vivo to release the desired parent compound; thus the double prodrugs extend the circulating half-life compared to the parent molecule (pp.6, 10–13).

Further, WO2002089789 [WO789; Citation 4A], discloses tetrapartate trimethyl lock prodrugs based on similar principle as the double prodrugs of WO483, but additionally incorporating a transport enhancer (Z moiety) between the parent molecule and the linker (analogous to L2 in WO483) attached to Ar moiety [Abstract; pp.4–8]. WO789 discloses that L1 (attached to ester substitution on phenyl ring) in Formula I can be -M-AA, wherein AA is an amino acid residue, preferably -C(=Y3)-CH2-CH2-X’, wherein X’ is O or NR17 [p.15]

Further, Simplicio et al., [doi: 10.3390/molecules13030519; Citation 4B] reviewed the published strategies for producing prodrugs, albeit for amines, and disclose the trimethyl lock and coumarin as spacers, wherein the phenolic -OH is protected by an ester/phosphate group that serves as an esterase/phosphatase sensitive biological triggering mechanism or a PEG-spacer-drug type prodrug [pp.530–531, 536–537]. They also note that another team prepared tripartite prodrug (double prodrug) that uses the coumarin system as a spacer between the drug (linked to the side chain) and a carrier group an amino acid, connected to the -OH of the coumarin [p.537].

The present Application WO2024249517 (WO517) claims, protease inhibitors of formulae I-XI (it may be noted that the compounds of WO517 represent carboxylate ester prodrugs of elunonavir), wherein the -OH group is linked to the TML-containing promoieties; -OH and -CH3 substitution on

phenyl group further derivatized to a phosphonooxy group and a substituted amide group (particularly amino acid or modified amino acid group, Claim 85), respectively (Claims 1–89). WO517 further claims pharmaceutical composition thereof along with additional therapeutic agents (e.g., lenacapavir), method of treating/preventing HIV therewith, use thereof, etc (Claims 90–150).

However, WO483 already discloses double prodrugs for hydroxyl/amine containing drugs, wherein the moiety attached to the phenolic O is first cleaved, followed by lactonization of the cleavable trialkyl (e.g., TML) linker to release the -OH-containing parent molecule. Also, Simplicio et al., disclose amino acids-TML lock-drug and PEG-spacer-drug type of prodrug strategies, albeit for amine drugs.

Thus, in light of the above, Claims 1–150 of WO517 lack inventive step.

Citation # 5 (Patent/utility model) (# uploaded documents: 0):

Country code:	Publication number:	Document kind code:
WO	2008/156632	A1

Patent Applicant/Patent Owner:	Title of invention:
Concert Pharmaceuticals, Inc.	Azapeptide derivatives

Link to document:
https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2008156632

Publication Date:	Filing Date:	Priority Date:
24 Dec 2008 (24/12/2008)	12 Jun 2008 (12/06/2008)	12 Jun 2007 (12/06/2007)

Source of Abstract:	Accession number:	Publication Date of Abstract:	Retrieval Date of Abstract:

Most relevant passages or drawings:	Relevant to Claims:
Abstract; pp.1–3, 9–15, 28–29, 42; Claims 8–18	1 to 150

Brief explanation of relevance:

WO2008156632 (WO632) relates to azapeptide compounds that are derivatives of an HIV protease inhibitor, particularly atazanavir (ATZ) sulphate (Abstract; pp. 1–3)

WO632 discloses and claims:
1. Markush Formula A, in some embodiments prodrugs of Markush Formula I, wherein the parent scaffold of deuterated ATZ has been derivatized at the secondary -OH with the -O-R5 modifications, wherein: (pp.2–3; 9–15, 28–29):
1a. R5, the prodrug moiety is –(CR6R7-O)n–R8;
1b. R6 and R7 are independently selected from H, C1-C6 alkyl, C3-C7 cycloalkyl, or taken together with the carbon to which they are attached to form a 3-7-membered cycloalkyl;
1c. R8 is (–C(O)-C1-C7 alkyl), -S(O)2-OH, -P(O)-(OH)2, or A-R11;
1d. When R8 is A-R11, A is an alpha-amino acid residue; and R11 is selected from C1-C6 alkyl, -C(O)-(C1-C7 alkyl), A-R12, where R12 is selected from H, C1-C6 alkyl, and -C(O)-(C1-C7 alkyl) (pp. 2, 9–10).
2. Though WO'632 provides data for the deuterated forms, it was found to be as potent as ATZ (pp. 4, 66–67). Nevertheless, the modifications envisaged in WO'632 are for prodrugs of ATZ derivatives (pp. 28–29)
3. An effective amount of the compound of formula A can be administered to a patient for treating HIV infection along with one or more second therapeutic agent (p.42; Claims 8–18).

Another patent application, WO2021188959 [WO959; attached as Citation 5A], discloses prodrugs (including those containing trimethyl-lock (TML) system) of Formula (I) of adenosine nucleosides for treating viral infections including HIV [Abstract]. WO959 discloses and/or claims Markush Formulae (I), (Ia) and (Ib), wherein a prodrug moiety may be attached at the 3' and 5' hydroxyl of the sugar moiety and/or the amino group of the nucleobase:
a. Two substitutions at hydroxy group of the sugar moiety are the R2 and R5 substitutions as follows:

(i) Compound of formula (Ib) where R2 and R5 represent -C(O)(Ra) wherein Ra is C1-C25 alkyl chain substituted with Rb, which is phenyl substituted with one to three groups of $-CH_3$ and -O-C(O) $-CH_3$ i.e. with the TML linkage [p. 23; Claims 1, 18–20, 23–26].

(ii) Compound of Formula (I) wherein R2 and R5 is -C(O)(Ra); Ra is (C1-C25) alkyl further substituted with Rb;

(iii) Rb is phenyl substituted with one–three groups chosen from Rf, -CH2-O-C(O)(Rf), and -O-C(O)(Rf) wherein Rf is C1–C18 chain [pp.18–19; Claims 30, 99, 101].

(iv) Compound of Formula (Ia) where R2 is -C(O)(Rb), and R5 is -C(O)(Ra); Ra is C1-C25 alkyl substituted with Rb; Rb is phenyl substituted with one to three groups from Rf and -O-C(O)(Rf); wherein Rf is a C1-C18 alkyl chain [pp.21–22; Claims 102, 125, 127].

b. The method of synthesis of compounds where the hydrogen of the hydroxy group or the amino group is substituted with 3,5-dimethyl-2-(2-methyl-4-oxohexan-2-yl)phenyl acetate. [pp.197–198; Compounds 14–16]. It may be noted that this is called as trimethyl lock (TML) system.

c. The antiviral activity of compounds, including compounds 14–16 for treating HIV [pp.214–219; Table 2].

d. Many compounds having TML promoieties at the hydroxyl group of the sugar moiety as well as at amino group of the nucleobase and the method of preparing these compounds [pp.32–35, 38–39, 43–44, 48–49, 221–223, 225–226, 228–229, 254–255; Examples P-C, P-D, P-E, P-F, P-K, P-L, P-Q, P-R, P-KKK, P-LLL].

e. The compounds or pharmaceutical composition thereof with additional therapeutic agents for the treatment of HIV [pp.51–151; Claims 128–132].

The present Application, WO2024249517 (WO517), claims compounds having Formula (I to XI) for the treatment of HIV infection (Abstract; p.3). The compound is substituted at hydroxy position of the parent drug by a TML promoiety and the phenyl ring is further derivatized by amino acids, phosphonooxy, sulphonyl group as prodrug approaches (Claim 1– 85). It further claims the pharmaceutical composition for the treatment or prevention of HIV (Claims 90–150).

However, WO632 already discloses the azapeptide scaffold that is in the present Application, WO517, and prodrugs thereof, wherein the hydroxy group is substituted (O-R5) and may be further substituted with an amino acid or phosphonooxy group. WO959 [Citation 5A] discloses the prodrug formation via substitution on the hydroxyl group with a TML linkage which is a known prodrug strategy. Both these applications disclose the method of treating HIV. Thus, it is obvious to a person skilled in the art to synthesize TML-containing prodrugs of compounds that are claimed in the present Application, WO517, by methods that are already known.

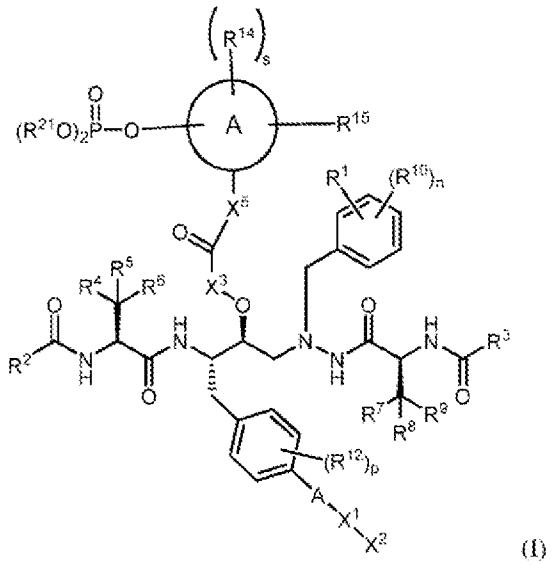
Thus, in light of WO632 and WO959 [Citations 5 and 5A], Claims 1 to 150 of WO517 lack inventive step

ADDITIONAL COMMENTS FOR WO 2024/249517

I. INTRODUCTION

WO2024/249517 (WO'517), an Application filed by Gilead Sciences, Inc., claims compounds of Markush Formula I (Claims 1–34), and its derivative Markush structures of Formulae II (Claim 35), III (Claim 36), IV (Claim 47), V (Claim 48), VI (Claim 52), VII (Claim 53), VIII (Claim 61), IX (Claim 62), X (Claim 65) and XI (Claim 69). As shown below, these are essentially prodrugs of atazanavir derivatives that were previously disclosed in WO2018145021, wherein the OH of the parent atazanavir derivatives are derivatized to form prodrugs.

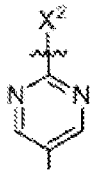
The following structures in **Figure A** and **Table A** show the different Markush structure Formulae claimed in the present Application, WO'517.



Formula I

Figure A: Markush Formula I claimed in Claim 1 of the present Application, WO'517

The present Application, WO'517, claims Markush Formula II to Markush Formula XI which are derivatives of Markush Formula I shown above in **Figure A**. Further, with respect to the derivatized Markush Formulae it may be noted that:

(1) Markush Formulae II and III are derivatives of Markush Formula II, wherein A is defined to be ethynyl, attached to X^1 which is  , which is further attached to X^2 which is  ; Formula III differs from Formula II, in that the R^2 and R^3 groups in Formula II are defined in Formula III

(2) Further, Markush formulae IV to XI have the A ring defined as the phenyl ring.

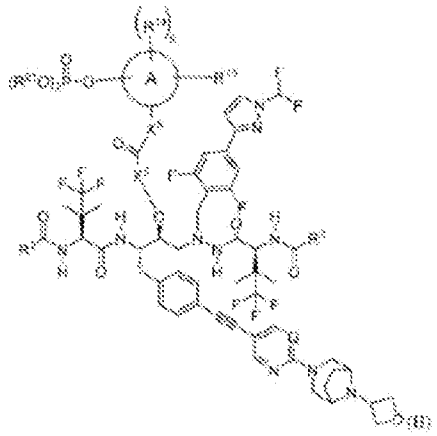
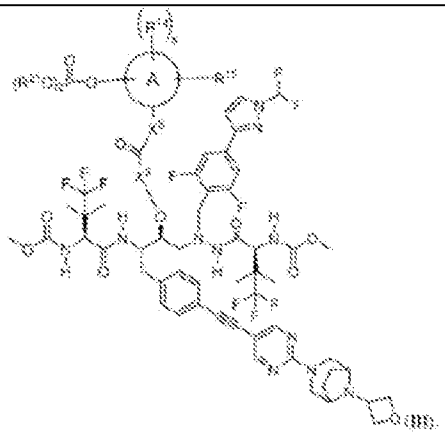
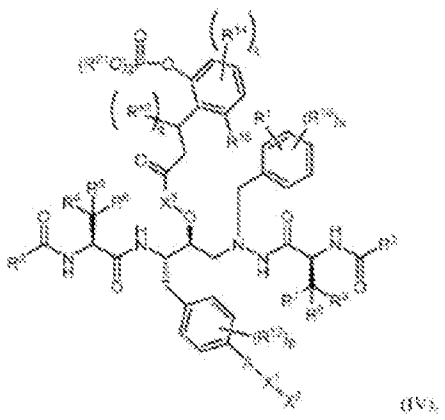
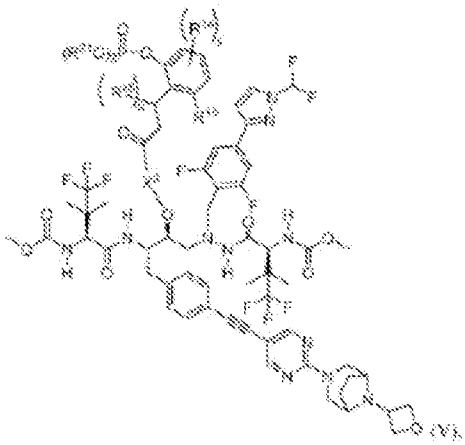
(3) Markush Formulae VI and VII define the specific position of the R^{14} and R^{15} substituents on the phenyl ring, whereas Formulae VIII and IX further define R^{15} as $-CH_2-Z^5$

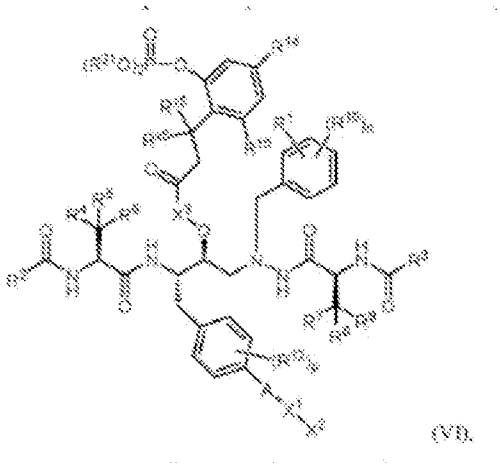
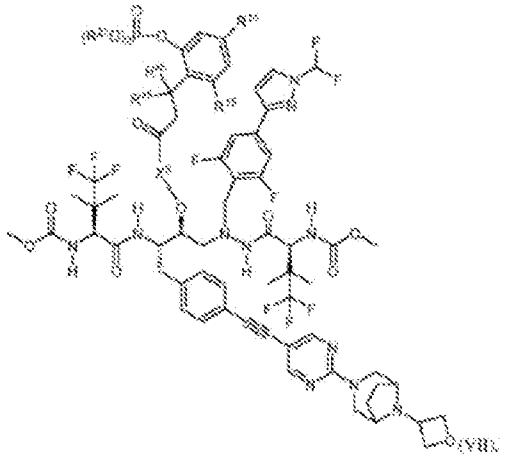
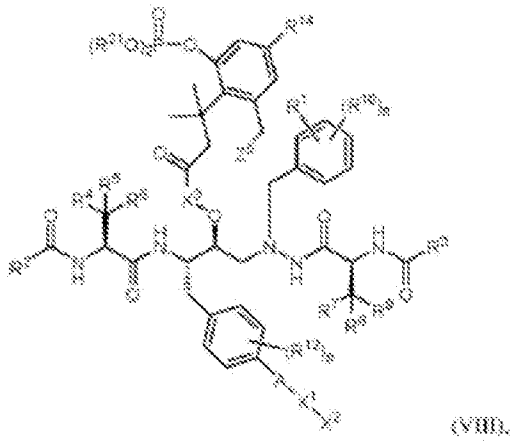
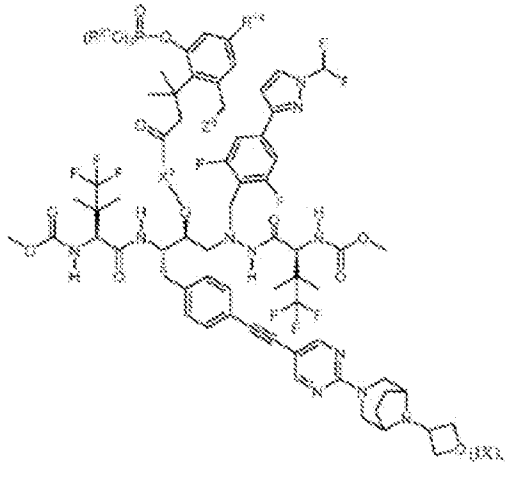
(4) Markush Formulae X and XI further define the R^{15} moiety as $-CH_2-C(O)-N(R^{24})(R^{25})$.

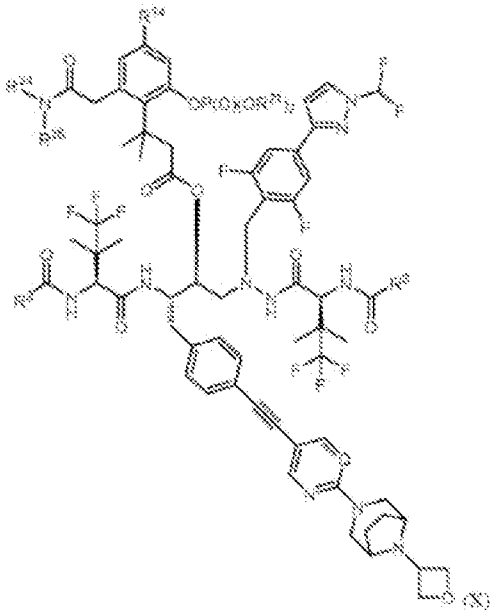
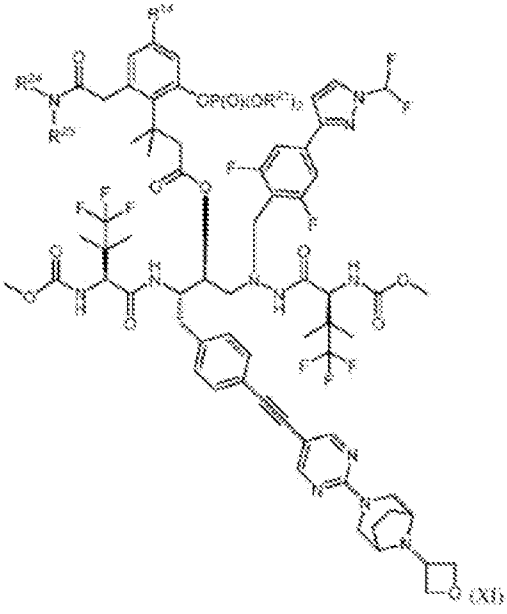
(5) Also, these Markush formulae II–XI have the A, X^1, X^2, R^2 and R^3 either defined or as variables.

The following table (**Table A**) shows the derivative Markush structures of Formula II–Formula XI of the present Application, WO'517.

Table A: Markush structures of Formula II-XI claimed in the present Application, WO'517

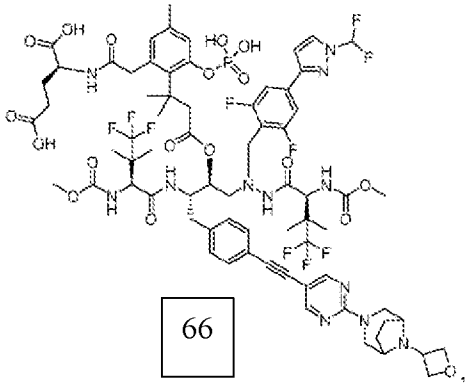
Sr. No.	Broad Markush formula claimed in WO'517	Narrowed down Markush structure claimed in WO'517
1	 Formula II (Claim 35)	 Formula III (Claim 36)
	Markush structure of formula II have variables R^1, R^4-R^{10}, R^{12} A, X^1, X^2 Markush variables substitution, wherein X^1 is a 6-membered ring containing N and variable Q.	Markush structure of Formula III has R^2, R^3 and X^1 wherein Q=N (derivative of Formula I)
2	 Formula IV (Claim 47)	 Formula V (Claim 48)

Sr. No.	Broad Markush formula claimed in WO'517	Narrowed down Markush structure claimed in WO'517
	Markush structure of Formula IV, wherein X^5 is defined as -CH2-	Markush structure of Formula is derivative of Formula IV, with the A, X^1 and X^2defined
3	 Formula VI (Claim 52)	 Formula VII (Claim 53)
	Markush structure of Formula VI has two R^{x5} variables substituted at the X^5	Markush structure of Formula VII is derivative of Formula VI with the A, X^1 and X^2 defined
4	 Formula VIII (Claim 61)	 Formula IX (Claim 62)

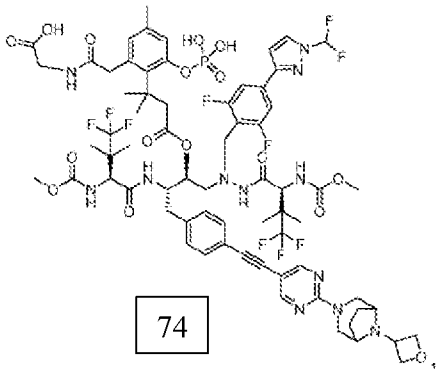
Sr. No.	Broad Markush formula claimed in WO'517	Narrowed down Markush structure claimed in WO'517
	Markush structure of Formula VIII has R^{15}, which is defined as -CH2-Z^5; R^{x5} is methyl.	Markush structure of Formula IX is derivative of Formula VIII, with the A, X^1 and X^2 defined
5	 Formula X (Claim 65)	 Formula XI (Claim 69)
	Markush structure of Formula X defines Z^5 as -C(O)N(R^{24})(R^{25})	Markush structure of Formula XI is specific derivative of Formula X, with the R^2 and R^3 defined

The present Application, WO'517, claims multiple possibilities for each of the variables in these Markush formulae, including the definitions for the A ring, A moiety, X^1–X^5, R^1–R^{28}, and further substitutions thereon such as R^{3A}, Z^5–Z^7, and the values for the variable integers p, n, s, etc. (Claims 1–83, 86–89). WO'517 claims a total of 113 specific compounds based on these XI Markush formulae and the different variables therein (Claim 84) and further narrows down to 5

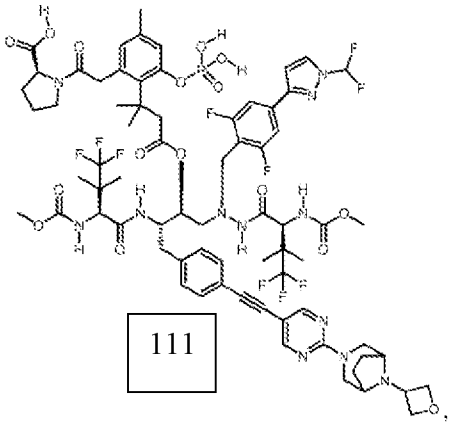
compounds (Compounds 32, 33, 66, 74, 111) (Claim 85) that are as shown in **Figure B** below.



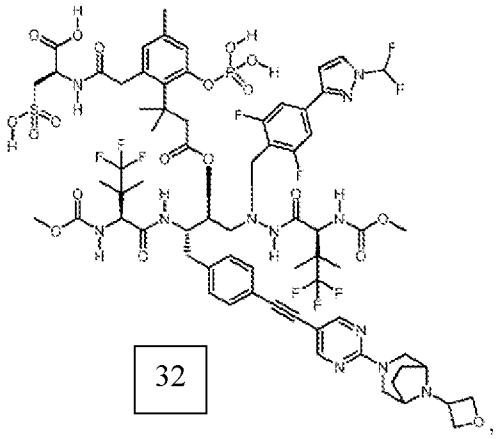
66



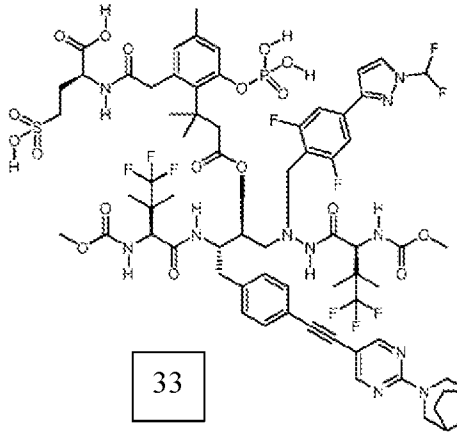
74



111



32



33

and , or a pharmaceutically acceptable

Figure B: Five specific compounds that have been claimed in Claim 85 of the present Application, WO'517

The present Application, WO'517, further claims:

a) A pharmaceutical composition comprising the compound of any one of Claims 1–89 or salt thereof, and a pharmaceutically acceptable excipient, and further comprising additional therapeutic agents such as lenacapavir, GS-CA1, etc. (Claims 90–101).
b) A method of treating or preventing HIV infection by administering the compound of any one of Claims 1–89 or a pharmaceutical composition of Claims 90–101 (Claims 102–115).
c) The claimed compound or the claimed pharmaceutical composition for use in therapy or for use in method of treating or preventing HIV infection (Claims 116–133).
d) Use of the claimed compound or the claimed pharmaceutical composition in the manufacture of a medicament for treating or preventing HIV infection in a heavily treatment-experienced patient, wherein the medicament is administered with additional therapeutic agents, either simultaneously or sequentially (Claims 134–150).

The present Application, WO'517, discloses that the compounds claimed and/or disclosed in the present Application, WO'517, are prodrugs, which may be metabolized in vivo to form one or more of the therapeutic compounds

described in the International Publication No. WO 2018/145021 [attached in the accompanying Third-Party Observation as Citation 1A].

WO'517 also discloses that the compounds claimed and/or disclosed in the present Application, WO'517, are prodrugs of compounds having the formula [para (164), p.86 of WO'517] as shown below in **Figure C**.

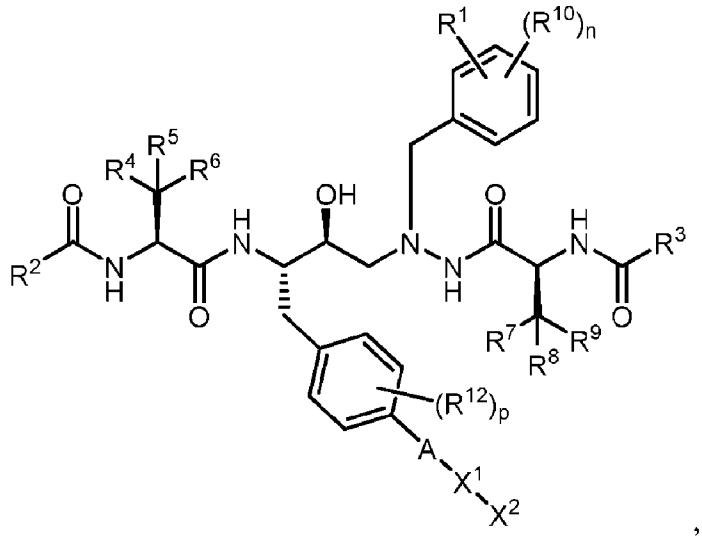


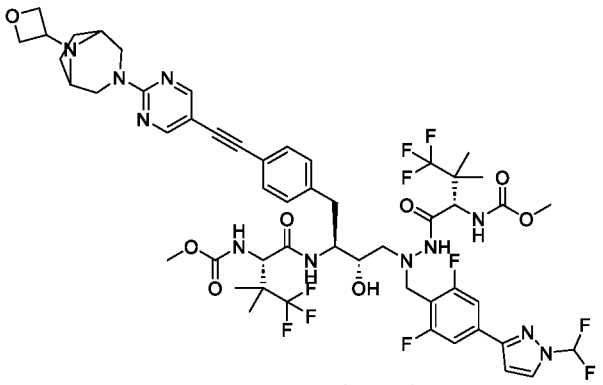
Figure C: Parent compound of prodrugs disclosed in the present Application, WO'517 (p.86)

It may be noted that the said formula shown in **Figure C** above covers the following HIV protease inhibitors, the structures of which have been shown below in **Figure D**:

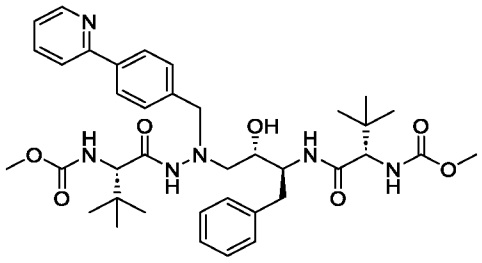
i) atazanavir[1] (ATV; pp.19–20 of the present Application, WO'517) developed by Bristol-Myers Squibb as the investigational drug BMS-232632

ii) elunonavir[2] developed by Gilead Sciences, Inc. and which is also known as GS-1156 or GS-PI-1.

[1] https://pubchem.ncbi.nlm.nih.gov/compound/Atazanavir#section=InChIKey
[2] https://pubchem.ncbi.nlm.nih.gov/compound/Elunonavir



elunonavir



Atazanavir

Thus, the compounds of the present Application, WO'517, are the prodrugs of the protease inhibitor compound ATV and its analogues, and more specifically prodrugs of elunonavir as shown in the accompanying Third-Party Observation (TPO).

The following Additional Comments are being filed along with the accompanying TPO to address the following points:

(i) Lack of unity of invention and

(ii) Lack of inventive step.

II. LACK OF UNITY OF INVENTION IN THE COMPOUNDS CLAIMED IN THE PRESENT APPLICATION, WO'517:

The 113 compounds claimed in Claim 84 of the present Application, WO'517, differ from each other predominantly in the substituents R^{14} and R^{15} (or $-CH_2-Z^5$) on the phenyl ring (i.e., the A ring) in the promoiety.

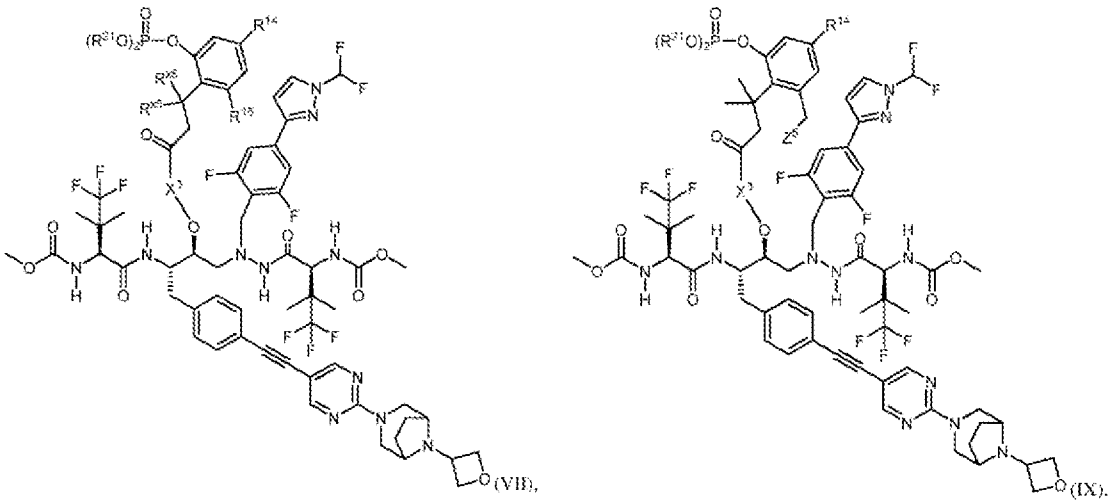


Figure E. Markush formulae represents the claimed compounds optimally

The several possibilities for R^{14} and R^{15} cannot be grouped together to form a single inventive concept.

Hence, the Claims of the present Application, WO'517, do not cover a single inventive concept, and therefore, lack unity of invention.

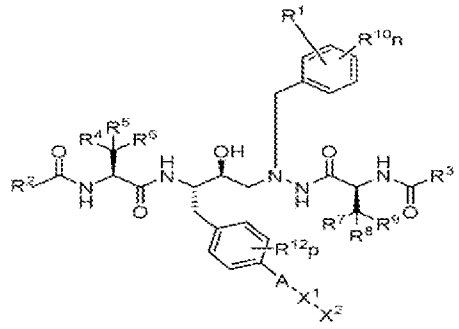
III. LACK OF INVENTIVE STEP FOR THE CLAIMS OF THE PRESENT APPLICATION, WO'517:

1. It may be noted that if the compounds of the present Application, WO'517, are broadly termed as prodrugs comprising the substituted phenyl ring with an ortho-phosphonooxy substitution, then such type of prodrugs are already disclosed in the prior art, in documents such as 1996 Dillon and 2017 Walther [Citations_3 and 3A respectively] as the phosphate-protected trimethyl lock type prodrugs, as is pointed out in the accompanying TPO.

2. The present Application, WO'517, admittedly claims prodrugs of certain *atazanavir* derivatives, including *elunonavir*. WO 2020/028272 [WO'272; attached as Citation 1 in the accompanying TPO) claims certain prodrugs of the same *atazanavir* derivatives, including *elunonavir*.

It may be noted that the *atazanavir* derivatives for which prodrugs are claimed in WO'272 as well as the present Application, WO'517, were disclosed and claimed previously by Gilead Sciences, Inc. in WO 2018/145021 [attached as Citation 1A in the accompanying TPO; Claim 1; see image below].

1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein:

A comparison of the Markush structure claimed in Claim 1 of WO 2018/145021 with the Markush structures claimed in WO272 [attached as Citation 1A in the accompanying TPO] and the present Application, WO'517, show that the OH in the parent molecule (*atazanavir* derivatives) has been derivatized to form different types of prodrugs in WO272 and in the present Application, WO'517 [compare structure above to the Markush structures in Table B added in the annexure].

As shown in the accompanying TPO, the Applicant, Gilead Sciences, Inc., has employed known prodrug strategies to obtain the prodrugs claimed in the present Application, WO'517.

Tables B and C, added in the annexure, provide a comparison of the similarity in the Markush structures claimed (for the parent molecule) and the similarity in the secondary claims, i.e., the claims for pharmaceutical composition, method of treatment and use, in WO272 [attached as Citation 1 in the accompanying TPO] and the present Application, WO517.

3. Further, as stated above in the Introduction, the present Application, WO'517, claims a pharmaceutical composition comprising the compound of any one of Claims 1–89 or salt thereof, and a pharmaceutically acceptable excipient, and further comprising additional therapeutic agents such as capsid inhibitors, including lenacapavir, etc. (Claims 90–101; Claims 98–100 disclosing structure of lenacapavir) and a method of treating or preventing HIV infection by administering the compound of any one of Claims 1–89 or a pharmaceutical composition of Claims 90–101 with such additional therapeutic agents (Claims 102–115, Claims 111–113 disclosing the structure of lenacapavir). Of these method claims, Claim 113 specifically claims such method of treating a human immunodeficiency virus (HIV) infection in a heavily treatment-experienced patient. With respect to this Claim 113 of the present Application, WO'517, it may be noted that lenacapavir was approved in the United States in 2022, and is marketed under the brand name Sunlenca[3]. The Label containing the prescribing information document (available at: https://www.gilead.com/-

[3] https://www.gilead.com/news/news-details/2022/sunlenca-lenacapavir-receives-fda-approval-as-a-first-in-class-twice-yearly-treatment-option-for-people-living-with-multi-drug-resistant-hiv#:~:text=FOSTER%20CITY%2C%20Calif.--%20%28BUSINESS%20WIRE%29--%20Gilead%20Sciences%2C%20Inc.,%28HTE%29%20adults%20with%20multi-drug%20resistant%20%28MDR%29%20HIV-1%20infection

/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.pdf) for the tablets for oral use and injection for subcutaneous use, also gives indication of usage. The Label discloses that Sunlenca is an HIV-1 capsid inhibitor, and is given in combination with other antiretrovirals, and "is indicated for the treatment of HIV-1 infection in heavily treatment-experienced adults with multi-drug resistant HIV-1 infection failing the current antiretroviral regimen due to resistance, intolerance, or safety considerations" and indicates such use in clinical trials (pp.1–2, 6–7, 14–16, 20–21). Therefore, the Label for Sunlenca, containing the prescribing information, already discloses that lenacapvir is used in heavily treatment-experienced patients, or multi-drug-resistant adults. Therefore, it is obvious that any pharmaceutical compositions containing lenacapavir as an additional therapeutic agents would also be indicated for use for the same purpose too. Thus, Claim 103 of the present Application, WO'517, lacks inventive step.

Thus, in light of the above tables of comparison and the accompanying TPO, Claims 1–150 of the present Application, WO'517, lack inventive step.

IV. CONCLUSION:

In light of the above, Claims 1 to 150 of the present Application, WO'517, suffer from lack unity of invention. Additionally, Claims 1 to 150 of the present Application, WO'517, fail for lack of inventive step.

ANNEXURE TO ADDITIONAL COMMENTS: TABLES OF COMPARISON OF WO 2020/028272 (PRIOR ART) AND THE PRESENT APPLICATION, WO 2024/249517

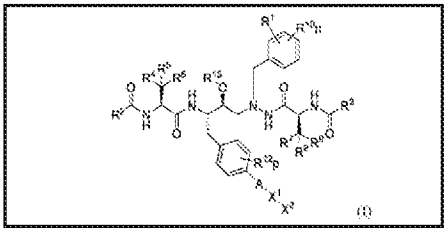
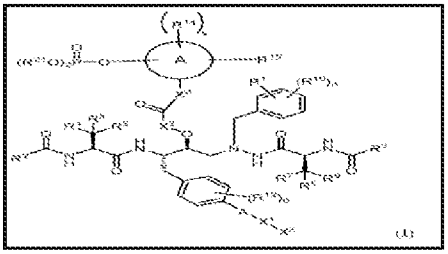
TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
Claim 1 A compound of Formula I  or a pharmaceutically acceptable salt thereof.	Claim 1 A compound of Formula I  or a pharmaceutically acceptable salt thereof.	The Markush structures are identical, i.e., the structures of the parent molecule (disclosed in WO 2018/145021) are identical; they differ only in the promoiety attached. The OH of the parent molecule is derivatised to form promoiety. Formula I of WO'272 has

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
		OR^{13} substitution as a prodrug forming moiety, while the present Application, WO'517, has another prodrug moiety substitution at an analogous position.
R^1 is a 5 to 10-membered heterocycle having 1 to 5 heteroatoms selected from N, O, and S, or a 5 to 10-membered heteroaryl having 1 to 5 heteroatoms selected from N, O, and S, wherein the 5 to 10-membered heterocycle or 5 to 10-membered heteroaryl is optionally substituted with 1 to 5 R^a groups;	R^1 is a 5 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, or a 5 to 10-membered heteroaryl having 1 to 5 heteroatoms selected from N, O, and S, wherein the 5 to 10-membered heterocyclyl or 5 to 10-membered heteroaryl is optionally substituted with 1 to 5 R^a groups;	The substituents defined for R^1 are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
R^2 and R^3 are each independently C_{1-4} alkyl, C_{3-6} cycloalkyl, O-R^{2A}, C_{1-2} alkyl-O-R^{2A}, N-$(R^{3A})_2$, or C1-2 alkyl-N-$(R^{3A})_2$, wherein each R^{2A} is independently C_{1-4} alkyl, C_{3-6} cycloalkyl, or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, wherein each R^{3A} is independently hydrogen, C_{1-4} alkyl, C_{3-6} cycloalkyl, or COO(R^e), wherein each R^e is independently hydrogen or C_{1-4} alkyl, and wherein each C_{3-6} cycloalkyl or 4 to 10-membered heterocyclyl is optionally substituted by 1 to 3 R^f groups, wherein each R^f is independently C1-2 alkyl or halogen;	R^2 and R^3 are each independently C_{1-4} alkyl, C_{3-6} cycloalkyl, O-R^{2A}, C_{1-2} alkyl-O-R^{2A}, N-$(R^{3A})_2$, or C1-2 alkyl-N-$(R^{3A})_2$, wherein each R^{2A} is independently C_{1-4} alkyl, C_{3-6} cycloalkyl, or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, wherein each R^{3A} is independently hydrogen, C_{1-4} alkyl, C_{3-6} cycloalkyl, or COO(R^e), wherein each R^e is independently hydrogen or C_{1-4} alkyl, and wherein each C_{3-6} cycloalkyl or 4 to 10-membered heterocyclyl is optionally substituted by 1 to 3 R^f groups, wherein each R^f is independently C1-2 alkyl or halogen;	The substituents defined for R^2 and R^3 are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
R^4 is hydrogen, halo, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;	R^4 is hydrogen, halo, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy;	The substituents defined for R^4 are identical.
R^7 is hydrogen, halo, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy	R^7 is hydrogen, halo, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy	The substituents defined for R^7 are identical.
R^5, R^6, R^8, and R^9 are each independently hydrogen, halo, C_{1-2} alkyl, C_{1-2} haloalkyl, or C_{3-6} cycloalkyl; and wherein two or more of R^4, R^5 and R^6 or two or more of R^7, R^8, and R^9 optionally join together to form one or more C_{3-6} cycloalkyl groups that are optionally substituted with 1 to 4 groups selected from halogen, C_{1-2} alkyl, and C_{1-2} haloalkyl;	R^5, R^6, R^8, and R^9 are each independently hydrogen, halo, C_{1-2} alkyl, C_{1-2} haloalkyl, or C_{3-6} cycloalkyl; and wherein two or more of R^4, R^5 and R^6 or two or more of R^7, R^8, and R^9 optionally join together to form one or more C_{3-6} cycloalkyl groups that are optionally substituted with 1 to 4 groups selected from halogen, C_{1-2} alkyl, and C_{1-2} haloalkyl;	The substituents defined for R^5, R^6, R^8, and R^9 are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
each R^{10} is independently halogen, cyano, C_{1-4} alkoxy, C_{1-6} alkyl, or C_{3-6} cycloalkyl;	each R^{10} is independently halogen, cyano, C_{1-4} alkoxy, C_{1-6} alkyl, or C_{3-6} cycloalkyl;	The substituents defined for R^{10} are identical.
n is 0 to 4	n is 0 to 4	Identical
each R^a is independently halogen, C_{1-4} alkyl, C_{1-4} alkyl with 1 to 2 groups selected from hydroxyl and C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S which is optionally substituted with R^{a1}, or O-R^{3B}, wherein R^{3B} is C_{3-6} cycloalkyl optionally substituted with R^{a1} or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S optionally substituted with R^{a1},	each R^a is independently halogen, C_{1-4} alkyl, C_{1-4} alkyl with 1 to 2 groups selected from hydroxyl and C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S which is optionally substituted with R^{a1}, or O-R^{3B}, wherein R^{3B} is C_{3-6} cycloalkyl optionally substituted with R^{a1} or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S optionally substituted with R^{a1},	The substituents defined for R^a are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
wherein each R^{a1} is independently C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{1-4} haloalkyl, or 4 to 8-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S;	wherein each R^{a1} is independently C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{1-4} haloalkyl, or 4 to 8-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S;	
A is ethynyl or a bond;	A is ethynyl or a bond;	The definition of "A" is identical.
X^1 is a 6 to 10-membered aryl or a 5 to 10-membered heteroaryl having 1 to 3 heteroatoms selected from N, O, and S, wherein each 6 to 10-membered aryl or 5 to 10-membered heteroaryl is optionally substituted with 1 to 4 R^b groups;	X^1 is a 6 to 10-membered aryl or a 5 to 10-membered heteroaryl having 1 to 3 heteroatoms selected from N, O, and S, wherein each 6 to 10-membered aryl or 5 to 10-membered heteroaryl is optionally substituted with 1 to 4 R^b groups;	The substituents defined for X^1 are identical.
X^2 is hydrogen or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, wherein the 4 to 10-membered heterocyclyl is optionally substituted with one R^{11} and optionally	X^2 is hydrogen or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, wherein the 4 to 10-membered heterocyclyl is optionally substituted with one R^{11} and optionally	The substituents defined for X^2 are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
substituted with 1 to 5 R^b groups;	substituted with 1 to 5 R^b groups;	
R^{11} is -C=O(R^c), CH2(R^d), $S(O)_{1-2}(C_{1-4}$ alkyl), $S(O)_{1-2}(C_{3-6}$ cycloalkyl), a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, or a 5 to 9-membered heteroaryl having 1 to 5 heteroatoms selected from N, O, and S, wherein each 4 to 10-membered heterocyclyl or 5 to 9-membered heteroaryl is optionally substituted with 1 to 5 R^b groups; each R^b is independently halogen, oxo, C_{1-4} alkyl, C_{1-4} alkyl with 1 to 2 groups selected from hydroxyl and C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} alkoxy, or COO(R^e);	R^{11} is -C=O(R^c), CH2(R^d), $S(O)_{1-2}(C_{1-4}$ alkyl), $S(O)_{1-2}(C_{3-6}$ cycloalkyl), a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S, or a 5 to 9-membered heteroaryl having 1 to 5 heteroatoms selected from N, O, and S, wherein each 4 to 10-membered heterocyclyl or 5 to 9-membered heteroaryl is optionally substituted with 1 to 5 R^b groups; each R^b is independently halogen, oxo, C_{1-4} alkyl, C_{1-4} alkyl with 1 to 2 groups selected from hydroxyl and C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} alkoxy, or COO(R^e);	The substituents defined for R^{11} are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
R^c is C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, $N(R^e)_2$, C_{3-6} cycloalkyl, or a 4 to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S, wherein the C_{3-6} cycloalkyl and the 4 to 6-membered heterocyclyl are optionally substituted by 1 to 5 R^b groups; R^d is $COO(R^e)$, $N(R^e)_2$, C_{3-6} cycloalkyl, or a 4 to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S, wherein the C_{3-6} cycloalkyl and the 4 to 6-memhered heterocyclyl is optionally substituted by 1 to 5 R^b groups;	R^c is C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, $N(R^e)_2$, C_{3-6} cycloalkyl, or a 4 to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S, wherein the C_{3-6} cycloalkyl and the 4 to 6-membered heterocyclyl are optionally substituted by 1 to 5 R^b groups; R^d is $COO(R^e)$, $N(R^e)_2$, C_{3-6} cycloalkyl, or a 4 to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S, wherein the C_{3-6} cycloalkyl and the 4 to 6-memhered heterocyclyl is optionally substituted by 1 to 5 R^b groups;	
each R^{12} is C_{1-2} alkyl, halo, -OC_{1-2} alkyl, or cyano;	each R^{12} is C_{1-2} alkyl, halo, -OC_{1-2} alkyl, or cyano;	The substituents defined for R^{12} are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
each p is 0 to 4;	each p is 0 to 4;	Identical
R^{13} is $-C(=O)R^{g1}$, $-C(=O)OR^{g2}$, or $-P(=O)(OR^{h})_2$; …	Ring A (6–10 membered aryl or 5–10 membered heteroaryl) which is substituted with $O-P=O(OR^{21})$, R^{14} and R^{15}; Wherein, R21 is H or $C_{1–6}$ alkyl; R14 and R15 is independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, $-OR^{23}$, $-C(O)R^{23}$, $-C(O)OR^{23}$, $-C(O)N(R^{24})(R^{25})$, $-OC(O)R^{23}$, $-OC(O)N(R^{24})(R^{25})$, $-P(O)(OR^{23})_2$, $-OP(O)(OR^{23})_2$, $-P(O)(R^{23})(OR^{23})$, or $-OP(O)(R^{23})(OR^{23})$, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with 1, 2, 3, or 4 Z^5; wherein Z^5 is independently C_{1-6} haloalkyl, $-OR^{23}$, $-C(O)R^{23}$, $-C(O)OR^{23}$, $-C(O)N(R^{24})(R^{25})$, $-OC(O)R^{23}$, -	The prodrug forming moiety differs.

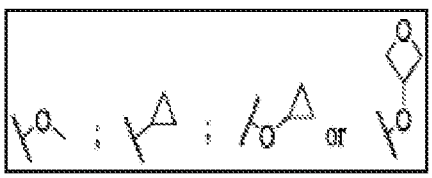
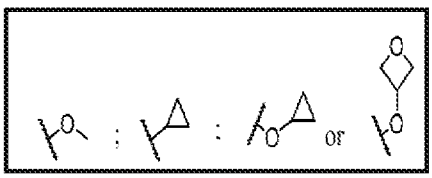
TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	$OC(O)N(R^{24})(R^{25})$, $-P(O)(OR^{23})_2$, $-OP(O)(OR^{23})_2$, $-P(O)(R^{23})(OR^{23})$, or $-OP(O)(R^{23})(OR^{23})$.	
2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each independently C_{1-4} alkyl, C_{3-6} cycloalkyl, or $O\text{-}R^{2A}$, wherein R^{2A} is C_{1-4} alkyl, C_{3-6} cycloalkyl, or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S.	2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each independently C_{1-4} alkyl, C_{3-6} cycloalkyl, or $O\text{-}R^{2A}$, wherein R^{2A} is C_{1-4} alkyl, C_{3-6} cycloalkyl, or a 4 to 10-membered heterocyclyl having 1 to 5 heteroatoms selected from N, O, and S.	The claims for the substituents on the Markush structure of the parent molecule are identical.
3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each independently: 	3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each independently: 	The claims for the substituents on the Markush structure of the parent molecule are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each methoxy.	4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each methoxy.	The claims for the substituents on the Markush structure of the parent molecule are identical.
5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl.	5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl.	The claims for the substituents on the Markush structure of the parent molecule are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^4 is C_{1-4} haloalkyl.	6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^4 is C_{1-4} haloalkyl.	The claims for the substituents on the Markush structure of the parent molecule are identical.
7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R^4 is CF_3.	7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R^4 is CF_3.	The claims for the substituents on the Markush structure of the parent molecule are identical.
8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R^7 is	8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R^7 is	The claims for the substituents on the Markush

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl.	hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl.	structure of the parent molecule are identical.
9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein R^7 is C_{1-4} haloalkyl.	9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein R^7 is C_{1-4} haloalkyl.	The claims for the substituents on the Markush structure of the parent molecule are identical.
10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein R^7 is CF_3.	10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein R^7 is CF_3.	The claims for the substituents on the Markush structure of the parent molecule are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
11. The compound of any one of claims to 10, or a pharmaceutically acceptable salt thereof, wherein R^5 and R^6 are C_{1-2} alkyl.	11. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein R^5 and R^6 are C_{1-2} alkyl.	The claims for the substituents on the Markush structure of the parent molecule are identical.
12. The compound of any one of claims to 11, or a pharmaceutically acceptable salt thereof, wherein R^5 and R^6 are methyl.	12. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein R^5 and R^6 are methyl.	The claims for the substituents on the Markush structure of the parent molecule are identical.
13. The compound of any one of claims to 12, or a pharmaceutically acceptable salt thereof, wherein R^8 and R^9 are C_{1-2} alkyl.	13. The compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, wherein R^8 and R^9 are C_{1-2} alkyl.	The claims for the substituents on the Markush structure of

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
		the parent molecule are identical.
14. The compound of any one of claims to 13, or a pharmaceutically acceptable salt thereof, wherein R^8 and R^9 are methyl.	14. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, wherein R^8 and R^9 are methyl.	The claims for the substituents on the Markush structure of the parent molecule are identical.
15. The compound of any one of claims to 14, or a pharmaceutically acceptable salt thereof, wherein n is 2.	15. The compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein n is 2.	The claims for the substituents on the Markush structure of the parent molecule are identical.

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
16. The compound of any one of claims to 15, or a pharmaceutically acceptable salt thereof, wherein each R^{10} is halogen.	16. The compound of any one of claims 1 to 15, or a pharmaceutically acceptable salt thereof, wherein each R^{10} is halogen.	The claims for the substituents on the Markush structure of the parent molecule are identical.
17. The compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt thereof, wherein each R^{10} is fluoro.	17. The compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt thereof, wherein each R^{10} is fluoro.	The claims for the substituents on the Markush structure of the parent molecule are identical.
18. The compound of any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein A is ethynyl.	18. The compound of any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein A is ethynyl.	The claims for the substituents on the Markush structure of

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
		the parent molecule are identical.
19. The compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein R^1 is a 5 to 6-membered heterocycle having 1 to 3 heteroatoms selected from N, O, and S, or a 5 to 6-membered heteroaryl having 1 to 3 heteroatoms selected from N, O, and S, wherein the 5 to 6-membered heterocycle or 5 to 6-membered heteroaryl is optionally substituted with 1 to 3 R^a groups.	19. The compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein R^1 is a 5- to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S, or a 5 to 6-membered heteroaryl having 1 to 3 heteroatoms selected from N, O, and S, wherein the 5 to 6-membered heterocyclyl or 5 to 6-membered heteroaryl is optionally substituted with 1 to 3 R^a groups.	The claims for the substituents on the Markush structure of the parent molecule are identical.
20. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein R^1 is a 5 to 6-membered heteroaryl having 1 to 3 heteroatoms	20. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein R^1 is a 5- to 6-membered heteroaryl having 1 to 3 heteroatoms	The claims for the substituents on the Markush structure of

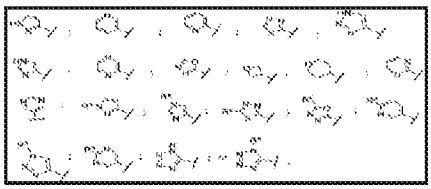
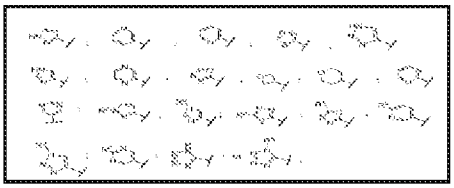
TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
selected from N, O, and S and is optionally substituted with 1 to 3 R^a groups.	selected from N, O, and S and is optionally substituted with 1 to 3 R^a groups.	the parent molecule are identical.
21. The compound of any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, wherein R^1 is independently: 	21. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein R1 is independently: 	The claims for the substituents on the Markush structure of the parent molecule are identical.

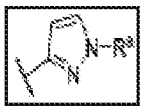
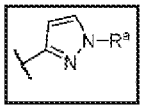
TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
22. The compound of any one of claims 1 to 21, or a pharmaceutically acceptable salt thereof, wherein R^1 is: 	22. The compound of any one of claims 1 to 21, or a pharmaceutically acceptable salt thereof, wherein R1 is: . 	The claims for the substituents on the Markush structure of the parent molecule are identical.
23. The compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, wherein R^a is C_{1-4} haloalkyl.	23. The compound of any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, wherein R^a is C_{1-4} haloalkyl.	The claims for the substituents on the Markush structure of the parent molecule are identical.
24. The compound of any one of claims 1 to 23, or a	24. The compound of any one of claims 1 to 23 or a	The claims for the substituents on the

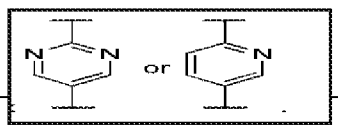
TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
pharmaceutically acceptable salt thereof, wherein R^a is: 	pharmaceutically acceptable salt thereof, wherein Ra is: 	Markush structure of the parent molecule are identical.
25. The compound of any one of claims 1 to 24, or a pharmaceutically acceptable salt thereof, wherein X^1 is a 6 -membered aryl or a 5 to 6-membered heteroaryl having 1 to 3 heteroatoms selected from N, O, and S, wherein each 6-membered aryl or 5 to 6-membered heteroaryl is optionally substituted with 1 to 4 R^b groups.	25. The compound of any one of claims 1 to 24, or a pharmaceutically acceptable salt thereof, wherein X^1 is a 6-membered aryl or a 5 to 6-membered heteroaryl having 1 to 3 heteroatoms selected from N, O, and S, wherein each 6-membered aryl or 5 to 6-membered heteroaryl is optionally substituted with 1 to 4 R^b groups.	The claims for the substituents on the Markush structure of the parent molecule are identical.
26. The compound of any one of claims 1 to 25, or a pharmaceutically acceptable salt thereof, wherein X^1 is:	26. The compound of any one of claims 1 to 25, or a pharmaceutically acceptable salt thereof, wherein X1 is: 	The claims for the substituents on the Markush structure of

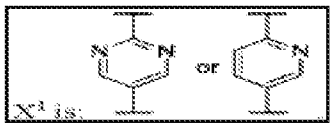
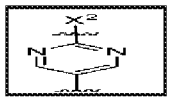
TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
		the parent molecule are identical.
27. The compound of any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, wherein X^1 is: 	27. The compound of any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, wherein X^1 is 	The claims for the substituents on the Markushstructure of the parent molecule are identical.
28. The compound of any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, wherein X^2 is a 4 to 10-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S and is optionally substituted with one R^{11} and optionally	28. The compound of any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, wherein X^2 is a 4 to 10-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S and is optionally substituted with one R^{11} and optionally	The claims for the substituents on the Markushstructure of the parent

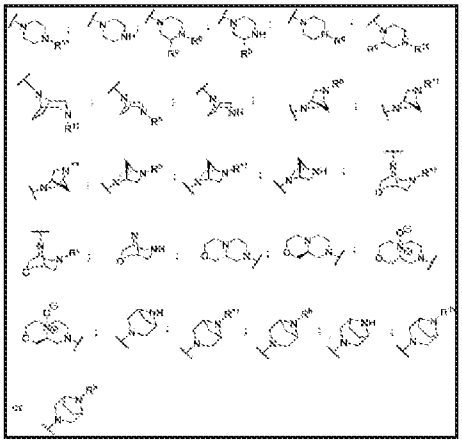
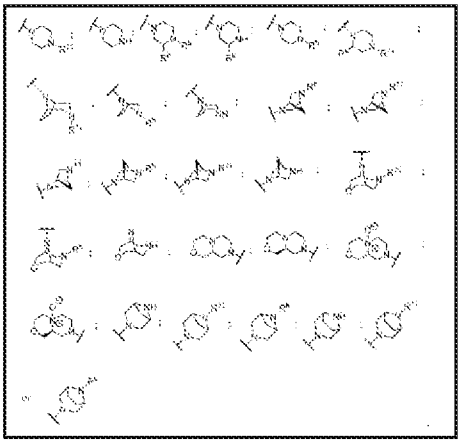
TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
substituted with 1 to 5 R^b groups.	substituted with 1 to 5 R^b groups.	molecule are identical.
29. The compound of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, wherein X^2 is: 	29. The compound of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, wherein X^2 is: 	The claims for the substituents on the Markush structure of the parent molecule are identical.
30. The compound of any one of claims 1 to 29, or a	30. The compound of any one of claims 1 to 29, or a	The claims for the

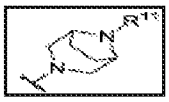
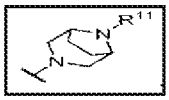
TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
pharmaceutically acceptable salt thereof, wherein X^2 is: 	pharmaceutically acceptable salt thereof, wherein X2 is: 	substituents on the Markush structure of the parent molecule are identical.
31. The compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, wherein R^{11} is 4 to 10-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S.	31. The compound of any one of claims 1 to 30, or a pharmaceutically acceptable salt thereof, wherein R^{11} is 4 to 10-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O, and S.	The claims for the substituents on the Markush structure of the parent molecule are identical.
32. The compound of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, wherein R^{11} is a 4 to 6-membered heterocycle having one oxygen.	32. The compound of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, wherein R^{11} is a 4 to 6-membered heterocyclyl having one oxygen.	The claims for the substituents on the Markush structure of the parent

TABLE B: COMPARISON OF PARENT MOLECULE FOR WHICH PRODRUGS ARE CLAIMED		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
		molecule are identical.
33. The compound of any one of claims 1 to 32, or a pharmaceutically acceptable salt thereof, wherein R^{11} is oxetan-3-yl.	33. The compound of any one of claims 1 to 32, or a pharmaceutically acceptable salt thereof, wherein R^{11} is oxetan-3-yl.	The claims for the substituents on the Markush structure of the parent molecule are identical.
34. The compound of any one of claims 1 to 33, or a pharmaceutically acceptable salt thereof, wherein p is 0.	34. The compound of any one of claims 1 to 33, or a pharmaceutically acceptable salt thereof, wherein p is 0.	The claims for the substituents on the Markush structure of the parent molecule are identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
56. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 55, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.	90. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1–89, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.	The claims are identical.
57. The pharmaceutical composition of claim 56, further comprising one, two, three, or four additional therapeutic agents. [see also Description pp. 49–63 of WO'272]	91. The pharmaceutical composition of claim 90, further comprising one, two, three, or four additional therapeutic agents.	The claims are identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
58. The pharmaceutical composition of claim 57, wherein the additional therapeutic agents are selected from the group consisting of combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, latency reversing agents, compounds that target the HIV capsid, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists,	92. The pharmaceutical composition of claim 91, wherein the one, two, three, or four additional therapeutic agents are selected from the group consisting of combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, HIV capsid inhibitors, <u>nucleocapsid protein 7 (NCp7) inhibitors, HIV</u> Tat <u>or Rev inhibitors, inhibitors of Tat-TAR-P-TEFb, immunomodulators, immunotherapeutic agents, antibody-drug conjugates, gene modifiers, gene editors (such as CRISPR/Cas9, zinc</u>	The listed additional therapeutic agents are very similar; the present Application, WO'517, having been filed later in time, has further therapeutic agents listed. The difference in the additional agents are underlined in the column for the present Application, WO'517.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-l viral infectivity factor inhibitors, TAT protein inhibitors, HIV-1 Nef modulators, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing inhibitors, Rev protein inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, retrocyclin modulators, CDK-9 inhibitors, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H	finger nucleases, homing nucleases, synthetic nucleases, TALENs), cell therapies (such as chimeric antigen receptor T-cell, CAR-T, and engineered T-cell receptors, TCR-T, autologous T-cell therapies, engineered B cells, NK cells), latency reversing agents, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, Fatty acid synthase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, HIV-1 Nef	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, pharmacokinetic enhancers, HIV gene therapy, and HIV vaccines, or any combinations thereof. [see also Description pp. 49–63 of WO'272]	modulators, TNF alpha ligand inhibitors, HIV Nef inhibitors, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, IFN antagonists, retrocyclin modulators, CD3 antagonists, CDK-4 inhibitors, CDK-6 inhibitors, CDK-9 inhibitors, Cytochrome P4503 inhibitors, CXCR4 modulators, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, HPK1 (MAP4K1) inhibitors, proprotein convertase PC9	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, mTOR complex 1 inhibitors, mTOR complex 2 inhibitors, P-Glycoprotein modulators, RNA polymerase modulators, TAT protein inhibitors, Prolyl endopeptidase inhibitors, Phospholipase A2 inhibitors, pharmacokinetic enhancers, HIV gene therapy, HIV vaccines, and anti-HIV peptides, or any combinations thereof.	
59. The pharmaceutical composition of claim 57, wherein the additional therapeutic agents are selected from the group consisting of HIV protease inhibiting compounds, HIV non-nucleoside inhibitors of	93. The pharmaceutical composition of claim 91, wherein the one, two, three, or four additional therapeutic agents are selected from the group consisting of combination drugs for HIV, other drugs for treating HIV,	The claims are almost identical. The difference in the additional

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
reverse transcriptase, HIV non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside inhibitors of reverse transcriptase, HIV nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, capsid polymerization inhibitors, pharmacokinetic enhancers, and other drugs for treating HIV, or any combinations thereof. [see also Description pp. 49–63 of WO'272]	HIV protease inhibitors, HIV reverse transcriptase inhibitors, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry (fusion) inhibitors, HIV maturation inhibitors, latency reversing agents, capsid inhibitors, immune-based therapies, PI3K inhibitors, HIV antibodies, bispecific antibodies, "antibody-like" therapeutic proteins, or any combinations thereof.	agents are underlined in the column for the present Application, WO'517. However, these have also been broadly disclosed in WO'272, the prior art document.
60. The pharmaceutical composition of any one of claims 57 to 59, wherein the additional therapeutic agents are selected from the group consisting of abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir	94. The pharmaceutical composition of any one of claims 91 to 93, wherein the one, two, three, or four additional therapeutic agents are selected from the group consisting of dolutegravir, cabotegravir, darunavir, bictegravir, elsulfavirine,	The claims are almost identical. The difference in the additional agents are

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
disoproxil hemifumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate. 94. The pharmaceutical composition of any one of claims 57 to 59, wherein the additional therapeutic agents are selected from the group consisting of abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide hemifumarate, emtricitabine, lamivudine, GS-9131, dolutegravir, and cabotegravir. [see also Description pp. 49–63 of WO'272]	<u>rilpivirine</u>, abacavir sulfate, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate, or a pharmaceutically acceptable salt thereof.	underlined in the column for the present Application, WO'517. However, it may be noted that these additional agents are known anti-HIV agents and have also been disclosed in WO'272.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
61. The pharmaceutical composition of any one of claims 57 to 60, wherein the additional therapeutic agents are selected from the group consisting of tenofovir alafenamide, tenofovir alafenamide fumarate and tenofovir alafenamide hemifumarate. 94. The pharmaceutical composition of any one of claims 57 to 59, wherein the additional therapeutic agents are selected from the group consisting of abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide hemifumarate, emtricitabine, lamivudine, GS-9131, dolutegravir, and cabotegravir.	95. The pharmaceutical composition of any one of claims 91 to 94, wherein the one, two, three, or four additional therapeutic agents are selected from abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide fumarate, and tenofovir alafenamide hemifumarate.	The claims are almost identical. The additional agents listed in Claim 95 of the present Application, WO'517, are listed in Claims 61 and 94 of WO'272.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
[see also Description pp. 49–63 of WO'272]		
61. The pharmaceutical composition of any one of claims 57 to 60, wherein the additional therapeutic agents are selected from the group consisting of tenofovir alafenamide, tenofovir alafenamide fumarate and tenofovir alafenamide hemifumarate. [see also Description pp. 49–63 of WO'272]	96. The pharmaceutical composition of any one of claims 91 to 95, wherein the one, two, three, or four additional therapeutic agents are selected from tenofovir alafenamide, tenofovir alafenamide fumarate, and tenofovir alafenamide hemifumarate.	The claims are identical.
95. The pharmaceutical composition of any one of claims 57 to 59 or 94, wherein the additional therapeutic agents are selected from the group consisting of	97. The pharmaceutical composition of any one of claims 91 to 94, wherein the one, two, three, or four additional therapeutic agents	The claims are identical.

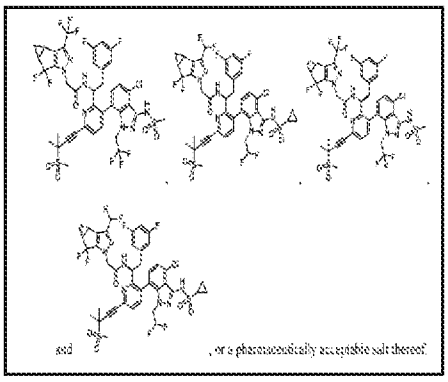
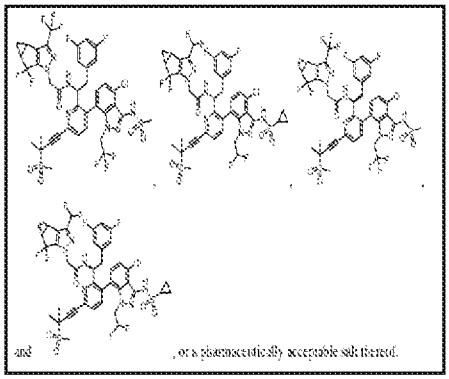
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
bictegravir, emtricitabine, and GS-9131. [see Description pp. 49–63 of WO'272; see p. 58 of WO'272]	are selected from bictegravir, emtricitabine, and GS-9131.	
82. The pharmaceutical composition of any one of claims of 57 to 59, wherein the additional therapeutic agents are selected from the group consisting of: 	98. The pharmaceutical composition of any one of claims 91 to 94, wherein the one, two, three, or four additional therapeutic agents are selected from: 	The claims are identical.

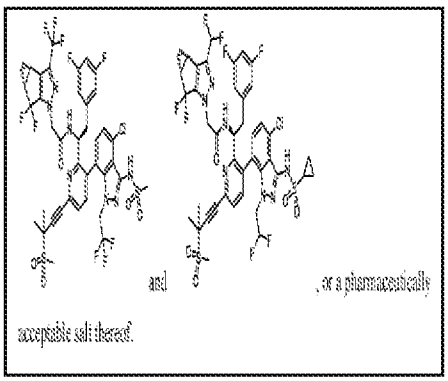
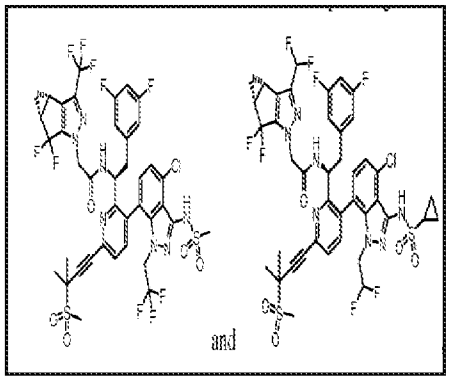
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
or a pharmaceutically acceptable salt thereof.	or a pharmaceutically acceptable salt thereof.	
83. The pharmaceutical composition of any one of claims 57 to 59 and 82, wherein the additional therapeutic agents are selected from the group consisting of:  	99. The pharmaceutical composition of any one of claims 91 to 94 and 98, wherein the one, two, three, or four additional therapeutic agents are selected from:  	The claims are identical.

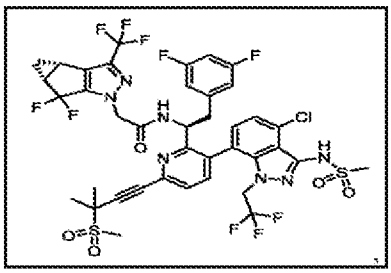
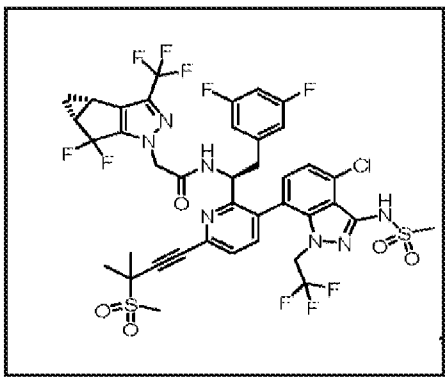
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
or a pharmaceutically acceptable salt thereof.	or a pharmaceutically acceptable salt thereof.	
84. The pharmaceutical composition of any one of claims 57 to 59, 82, and 83, wherein the additional therapeutic agent is:  or a pharmaceutically acceptable salt thereof.	100. The pharmaceutical composition of any one of claims 91 to 94 and 98 to 99, wherein the one, two, three, or four additional therapeutic agent is:  , or a pharmaceutically acceptable salt thereof.	The claims are identical.
85. The pharmaceutical composition of any one of claims 57 to 59, 82, and 83,	101. The pharmaceutical composition of any one of claims 91 to 94 and 98 to 99,	The claims are identical.

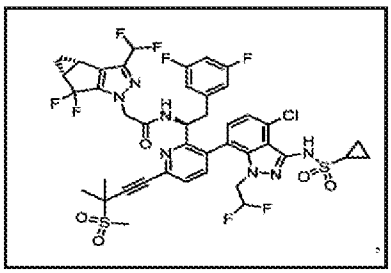
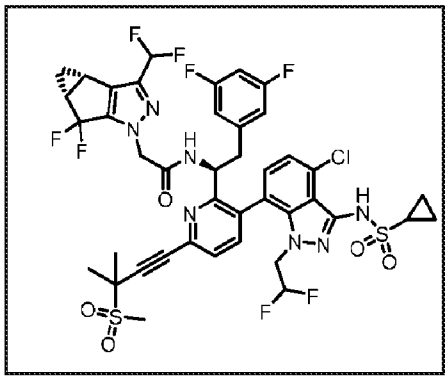
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
wherein the additional therapeutic agent is:  or a pharmaceutically acceptable salt thereof.	wherein the one, two, three, or four additional therapeutic agent is:  or a pharmaceutically acceptable salt thereof.	
62. A method of treating or preventing a human immunodeficiency virus (HIV) infection comprising administering a therapeutically effective amount of a compound of any one of claims 1 to 55, or a	102. A method of treating or preventing a human immunodeficiency virus (HIV) infection in a patient in need thereof comprising administering to the patient a therapeutically effective amount of a compound of	The claims are almost identical, except that the present Application, WO'517, also claims such

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
pharmaceutically acceptable salt thereof, to a subject in need thereof.	any one of claims 1 to 89, or a pharmaceutically acceptable salt thereof, to a subject in need thereof, or a pharmaceutical composition of any one of claims 90 to 101. 103. A method of treating a human immunodeficiency virus (HIV) infection in a heavily treatment-experienced patient, the method comprising administering to the patient a therapeutically effective amount of the compound of any one of claims 1 to 89, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 90 to 101.	method with a pharmaceutical composition.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
63. The method of claim 62, wherein the method comprises administering the compound, or a pharmaceutically acceptable salt thereof, in combination with one, two, three, or four additional therapeutic agents.	104. The method of claim 102 or claim 103, wherein the method comprises administering the compound, or a pharmaceutically acceptable salt thereof, in combination with one, two, three, or four additional therapeutic agents.	The claims are identical.
64. The method of claim 63, wherein the additional therapeutic agents are selected from the group consisting of combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation	105. The method of claim 104, wherein the one, two, three, or four additional therapeutic agents are selected from the group consisting of combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry	The listed additional therapeutic agents are very similar; the present Application, WO'517, having been filed later in time, has further therapeutic agents listed.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
inhibitors, latency reversing agents, compounds that target the HIV capsid, immune-based therapies, phosphatidylinositol 3 -kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and"antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, TAT protein inhibitors, HIV-1 Nef modulators, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing inhibitors, Rev protein inhibitors, integrin antagonists, nucleoprotein	inhibitors, HIV maturation inhibitors, HIV capsid inhibitors, nucleocapsid protein 7 (NCp7) inhibitors, HIV Tat or Rev inhibitors, inhibitors of Tat-TAR-P-TEFb, immunomodulators, immunotherapeutic agents, antibody-drug conjugates, gene modifiers, gene editors (such as CRISPR/Cas9, zinc finger nucleases, homing nucleases, synthetic nucleases, TALENs), cell therapies (such as chimeric antigen receptor T-cell, CAR-T, and engineered T-cell receptors, TCR-T, autologous T-cell therapies, engineered B cells, NK cells), latency reversing agents, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists,	The difference in the additional agents are underlined in the column for the present Application, WO'517.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, retrocyclin modulators, CDK-9 inhibitors, dendritic IC AM- 3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, pharmacokinetic enhancers, HIV gene therapy, and HIV vaccines, or any combinations thereof.	peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, Fatty acid synthase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, HIV-1 Nef modulators, TNF alpha ligand inhibitors, HIV Nef inhibitors, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, IFN antagonists, retrocyclin modulators, CD3 antagonists, CDK-4 inhibitors, CDK-6 inhibitors, CDK-9 inhibitors, Cytochrome P4503 inhibitors, CXCR4 modulators, dendritic	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, HPK1 (MAP4K1) inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, mTOR complex 1 inhibitors, mTOR complex 2 inhibitors, P-Glycoprotein modulators, RNA polymerase modulators, TAT protein inhibitors, Prolyl endopeptidase inhibitors, Phospholipase A2 inhibitors, pharmacokinetic enhancers, HIV gene therapy, HIV vaccines, and anti-HIV peptides, or any combinations thereof.	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
65. The method of claim 63 or 64, wherein the additional therapeutic agents are selected from the group consisting of HIV protease inhibiting compounds, HIV non-nucleoside inhibitors of reverse transcriptase, HIV non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside inhibitors of reverse transcriptase, HIV nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, capsid polymerization inhibitors, pharmacokinetic enhancers, and other drugs for treating HIV, or any combinations thereof.	106. The method of claim 104 or claim 105, wherein the one, two, three, or four additional therapeutic agents are selected from the group consisting of combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV reverse transcriptase inhibitors, HIV integrase inhibitors, <u>HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry (fusion) inhibitors, HIV maturation inhibitors, latency reversing agents</u>, capsid inhibitors, immune-based therapies, PI3K inhibitors, HIV antibodies, bispecific antibodies, and "antibody-like" therapeutic proteins, or any combinations thereof.	The claims are almost identical. The difference in the additional agents are underlined in the column for the present Application, WO'517. However, these have also been disclosed in WO'272, the prior art document.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
66. The method of any one of claims 63 to 65, wherein the additional therapeutic agents are selected from the group consisting of abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate.	107. The method of any one of claims 104 to 106, wherein the one, two, three, or four additional therapeutic agents are selected from the group consisting of dolutegravir, cabotegravir, darunavir, bictegravir, elsulfavirine, rilpivirine, abacavir sulfate, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate, or a pharmaceutically acceptable salt thereof.	The claims are almost identical. The difference in the additional agents are underlined in the column for the present Application, WO'517. However, it may be noted that these additional agents are known anti-HIV agents and most of them have also been disclosed in WO'272.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
67. The method of any one of claims 63 to 66, wherein the additional therapeutic agents are selected from the group consisting of tenofovir alafenamide, tenofovir alafenamide fumarate and tenofovir alafenamide hemifumarate. 96. The method of any one of claims of 63 to 65, wherein the additional therapeutic agents are selected from the group consisting of abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide hemifumarate, emtricitabine, lamivudine, GS-9131, dolutegravir, and cabotegravir.	108. The method of any one of claims 104 to 107, wherein the one, two, three, or four additional therapeutic agents are selected from abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide fumarate, and tenofovir alafenamide hemifumarate.	The claims are almost identical. The agents listed in Claim 108 of the present Application, WO'517, are listed in Claims 67 and 96 of WO'272.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
67. The method of any one of claims 63 to 66, wherein the additional therapeutic agents are selected from the group consisting of tenofovir alafenamide, tenofovir alafenamide fumarate and tenofovir alafenamide hemifumarate.	109. The method of any one of claims 104 to 108, wherein the one, two, three, or four additional therapeutic agents are selected from tenofovir alafenamide, tenofovir alafenamide fumarate, and tenofovir alafenamide hemifumarate.	The claims are identical.
97. The method of any one of claims of 63 to 65 and 96, wherein the additional therapeutic agents are selected from the group consisting of bictegravir, emtricitabine, and GS-9131. [see Description pp. 49–63 of WO'272; see p. 58 of WO'272]	110. The method of any one of claims 104 to 106, wherein the one, two, three, or four additional therapeutic agents are selected from bictegravir, emtricitabine, and GS-9131.	The claims are identical.

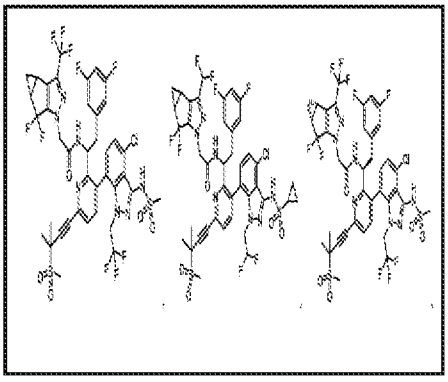
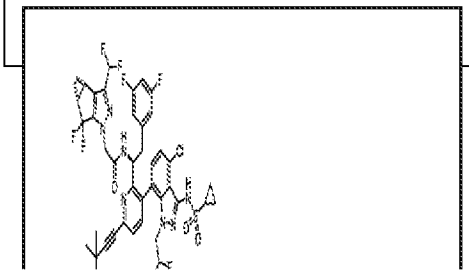
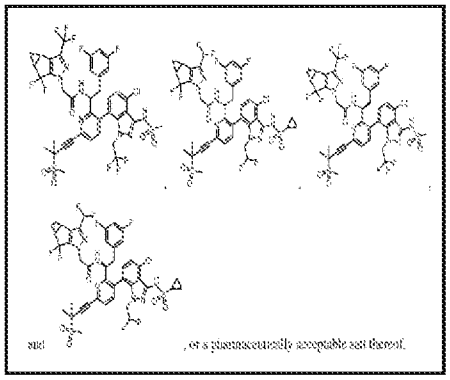
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
86. The method of any one of claims of 63 to 65, wherein the additional therapeutic agents are selected from the group consisting of:  	111. The method of any one of claims 104 to 106, wherein the one, two, three, or four additional therapeutic agents are selected from:  or a pharmaceutically acceptable salt thereof.	The claims are identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**

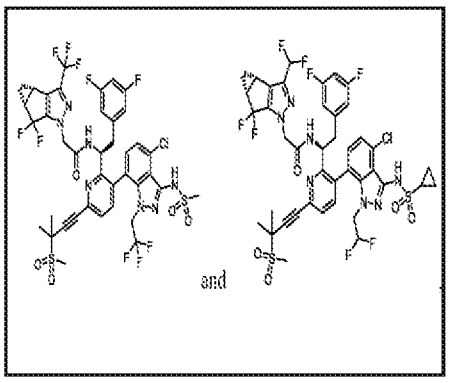
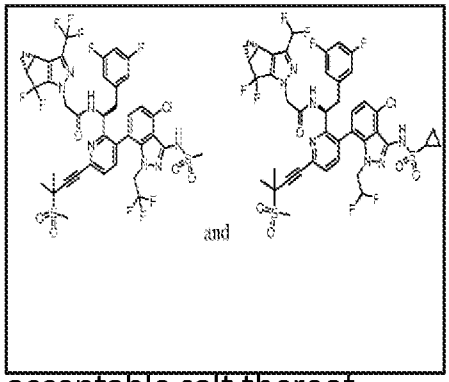
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
87. The method of any one of claims 63 to 65 and 86, wherein the additional therapeutic agents are selected from the group consisting of:  or a pharmaceutically acceptable salt thereof.	112. The method of any one of claims 104 to 106 and 111, wherein the one, two, three, or four additional therapeutic agents are selected from:  acceptable salt thereof. or a pharmaceutically acceptable salt thereof.	The claims are identical.

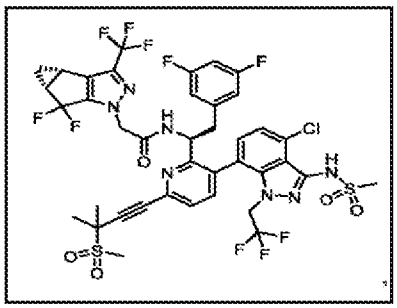
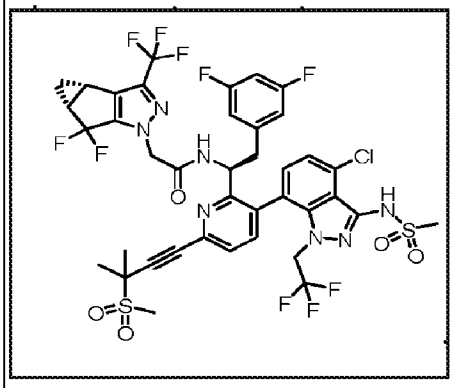
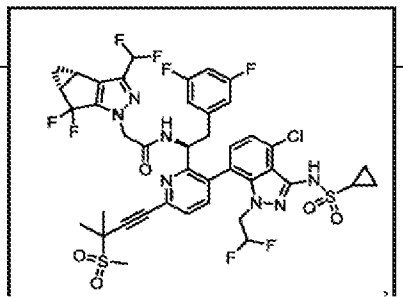
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
88. The method of any one of claims 63 to 65, 86, and 87, wherein the additional therapeutic agent is:  or a pharmaceutically acceptable salt thereof.	113. The method of any one of claims 104 to 106 and 111 to 112, wherein the one, two, three, or four additional  or a pharmaceutically acceptable salt thereof.	The claims are identical.
89. The method of any one of claims 63 to 65, 86, and 87, wherein the additional therapeutic agent is: 	114. The method of any one of claims 104 to 106 and 111 to 112, wherein the one, two, three, or four additional therapeutic agent is:	The claims are identical.

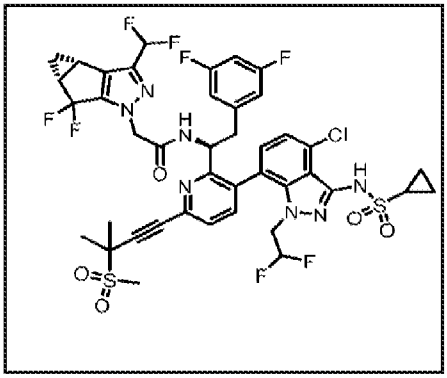
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
or a pharmaceutically acceptable salt thereof.	 or a pharmaceutically acceptable salt thereof.	
	115. The method of any one of claims 102 to 114, wherein the patient is a human.	
68. A compound of any one of claims 1 to 55, or a pharmaceutically acceptable	116. A <u>therapeutically effective amount of</u> a compound of any one of claims 1 to 89, or a	The claims are identical, except that the present

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
salt thereof, for use in therapy.	pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 90 to 101, for use in therapy.	Application, WO'517, also claims such use with a pharmaceutical composition.
69. A compound of any one of claims 1 to 55, or a pharmaceutically acceptable salt thereof, for use in a method of treating or preventing a human immunodeficiency virus (HIV) infection comprising administering a therapeutically effective amount of the compound to a subject in need thereof. [0128] In certain embodiments, the use of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, for the manufacture of a	117. A compound of any one of claims 1 to 89, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 90 to 101, for use in a method of treating or preventing a human immunodeficiency virus (HIV) infection in a patient in need thereof, the method comprising administering to the patient a therapeutically effective amount of the compound to a subject in need thereof, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition.	The claims are identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
medicament for an Retroviridae viral infection (e.g., an HIV infection) in a subject (e.g, a human) is disclosed. [see p. 44 of WO'272]	*135. Use of a compound of any one of claims 1 to 89, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 90 to 101, in the manufacture of a medicament for treating or preventing a human immunodeficiency virus (HIV) infection in a patient.*	
	118. A compound of any one of claims 1 to 89, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 90 to 101, for use in a method of treating a human immunodeficiency virus (HIV) infection in a heavily treatment-experienced patient, the method	Lenacapavir, an HIV capsid inhibitor, is one of the drugs claimed to be administered in combination with compounds of the present Application,

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	comprising administering to the patient a therapeutically effective amount of the compound, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition. *136. Use of a compound of any one of claims 1 to 89, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 90 to 101, in the manufacture of a medicament for treating a human immunodeficiency virus (HIV) infection in a heavily treatment-experienced patient.*	WO'517 [Claims 98–100, 111–113 of WO'517]. The Label, prescribing information for Sunlenca (lenacapavir) discloses that it is indicated for use in heavily treatment experienced patients.[4] Therefore, use of the claimed drugs in combination with lenacapavir in heavily treatment

[4] The Label for Sulenca states that Sunlenca (i.e., lenacapavir), is an HIV-1 capsid inhibitor, given in combination with other antiretrovirals and "is indicated for the treatment of HIV-1 infection in heavily treatment-experienced adults with multi-drug resistant HIV-1 infection" and indicates such use in clinical trials (pp.1–2, 6–7, 14–16, 20–21). *Available at*: https://www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.pdf.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
		experienced patients is obvious.
70. The compound for use according to claim 69, wherein the method comprises administering one, two, three or four additional therapeutic agents.	119. The compound for use of claim 117 or claim 118, wherein the method further comprises administering a therapeutically effective amount of one, two, three, or four additional therapeutic agents, or a pharmaceutically acceptable salt thereof. *137. The use of claim 135 or claim 136, wherein the medicament is administered with one, two, three or four additional therapeutic agents.*	The claims are identical.
71. The compound for use as claimed in claim 70, wherein the additional therapeutic agents are administered simultaneously with the	120. The compound for use of claim 119, wherein the additional therapeutic agents are administered simultaneously with the	The claims are identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
compound of any one of claims 1 to 57, or a pharmaceutically acceptable salt thereof.	compound, or a pharmaceutically acceptable salt thereof. *138. The use of claim 137, wherein the one, two, three, or four additional therapeutic agents are administered simultaneously with the medicament.*	
72. The compound for use as claimed in claim 70, wherein the compound of any one of claims 1 to 57 is combined with the additional therapeutic agents in a unitary dosage form for simultaneous administration.	121. The compound for use of claim 119, wherein the compound, or a pharmaceutically acceptable salt thereof, is combined with the additional therapeutic agents in a unitary dosage form for simultaneous administration. *139. The use of claim 137, wherein the medicament is combined with the one, two, three, or four additional*	The claims are identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	therapeutic agents in a unitary dosage form for simultaneous administration.	
73. The compound for use as claimed in claim 70, wherein the compound of any one of claims 1 to 57 is administered and the additional therapeutic agents are administered sequentially.	122. The compound for use of claim 119, wherein the compound, or a pharmaceutically acceptable salt thereof, and the additional therapeutic agents are administered sequentially. *140. The use of claim 137, wherein the medicament and the one, two, three, or four additional therapeutic agents are administered sequentially.*	The claims are identical.
74. The compound for use according to claim 70, wherein the additional therapeutic agents are selected from the group consisting of combination	123. The compound for use of any one of claims 119 to 122, wherein the one, two, three, or four additional therapeutic agents are selected from the group consisting of	The listed additional therapeutic agents are very similar; the present

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, latency reversing agents, compounds that target the HIV capsid, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody - like" therapeutic proteins, HIV pl7 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor,	combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, HIV capsid inhibitors, <u>nucleocapsid protein 7 (NCp7) inhibitors</u>, <u>HIV</u> Tat <u>or Rev inhibitors, inhibitors of Tat-TAR-P-TEFb, immunomodulators, immunotherapeutic agents, antibody-drug conjugates, gene modifiers, gene editors (such as CRISPR/Cas9, zinc finger nucleases, homing nucleases, synthetic nucleases, TALENs), cell therapies (such as chimeric antigen receptor T-cell, CAR-T, and engineered T-cell</u>	Application, WO517, having been filed later in time, has further therapeutic agents listed. The difference in the additional agents are underlined in the column for the present Application, WO'517.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, TAT protein inhibitors, HIV-1 Nef modulators, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-l splicing inhibitors, Rev protein inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, retrocyclin modulators, CDK-9 inhibitors, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, proprotein convertase PC9 stimulators, ATP dependent	receptors, TCR-T, autologous T-cell therapies, engineered B cells, NK cells), latency reversing agents, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, Fatty acid synthase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, HIV-1 Nef modulators, TNF alpha ligand inhibitors, HIV Nef inhibitors, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing inhibitors,	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, pharmacokinetic enhancers, HIV gene therapy, and HIV vaccines, or any combinations thereof.	integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, IFN antagonists, retrocyclin modulators, CD3 antagonists, CDK-4 inhibitors, CDK-6 inhibitors, CDK-9 inhibitors, Cytochrome P4503 inhibitors, CXCR4 modulators, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, HPK1 (MAP4K1) inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors,	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	mTOR complex 1 inhibitors, mTOR complex 2 inhibitors, P-Glycoprotein modulators, RNA polymerase modulators, TAT protein inhibitors, Prolyl endopeptidase inhibitors, Phospholipase A2 inhibitors, pharmacokinetic enhancers, HIV gene therapy, HIV vaccines, and anti-HIV peptides, or any combinations thereof. *141. The use of any one of claims 137 to 140, wherein the one, two, three, or four additional therapeutic agents are selected from combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic*	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, latency reversing agents, compounds that target the HIV capsid, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, TAT protein inhibitors, HIV-1 Nef modulators, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	inhibitors, Rev protein inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, retrocyclin modulators, CDK-9 inhibitors, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, pharmacokinetic enhancers, HIV gene therapy, and HIV vaccines, or any combinations thereof.	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
75. The compound for use according to claim 70, wherein the additional therapeutic agents are selected from the group consisting of HIV protease inhibiting compounds, HIV non-nucleoside inhibitors of reverse transcriptase, HIV non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside inhibitors of reverse transcriptase, HIV nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, capsid polymerization inhibitors, pharmacokinetic enhancers, and other drugs for treating HIV, or any combinations thereof.	124. The compound for use of any one of claims 119 to 123, wherein the one, two, three, or four additional therapeutic agents are selected from the group consisting of <u>combination drugs for HIV, other drugs for treating HIV</u>, HIV protease inhibitors, HIV reverse transcriptase inhibitors, HIV integrase inhibitors, HIV <u>non-catalytic site (or allosteric)</u> integrase inhibitors, <u>HIV entry (fusion) inhibitors, HIV maturation inhibitors, latency reversing agents</u>, capsid inhibitors, immune-based therapies, <u>PI3K inhibitors, HIV antibodies, bispecific antibodies, and "antibody-like" therapeutic proteins</u>, or any combinations thereof. *142. The use of any one of claims 137 to 140, wherein the one, two, three, or four*	The claims are almost identical. The difference in the additional agents are underlined in the column for the present Application, WO'517. However, these have also been broadly disclosed in WO'272, the prior art document.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	additional therapeutic agents are selected from HIV protease inhibiting compounds, HIV non-nucleoside inhibitors of reverse transcriptase, HIV non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside inhibitors of reverse transcriptase, HIV nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, capsid polymerization inhibitors, pharmacokinetic enhancers, and other drugs for treating HIV, or any combinations thereof.	
76. The compound for use according to claim 70, wherein the compound is combined with abacavir sulfate, bictegravir, tenofovir,	125. The compound for use of any one of claims 119 to 124, wherein the one, two, three, or four additional therapeutic agents are selected from the	The claims are almost identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, or tenofovir alafenamide hemifumarate. 78. The compound for use according to claim 70, wherein the compound is combined with tenofovir disoproxil, tenofovir disoproxil hemifumarate or tenofovir disoproxil fumarate. 98. The compound for use according to any one of claims 70 to 75, wherein the compound is combined with an additional therapeutic agent selected from the group consisting of abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide,	group consisting of dolutegravir, cabotegravir, <u>darunavir</u>, bictegravir, <u>elsulfavirine</u>, <u>rilpivirine</u>, abacavir sulfate, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate, or a pharmaceutically acceptable salt thereof. *143. The use of any one of claims 137 to 142, wherein the one, two, three, or four additional therapeutic agents are selected from abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide fumarate, tenofovir alafenamide hemifumarate, emtricitabine, lamivudine, GS-*	The difference in the additional agents are underlined in the column for the present Application, WO'517. However, it may be noted that these additional agents are known anti-HIV agents and most of them have also been disclosed in WO'272.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
tenofovir alafenamide hemifumarate, emtricitabine, lamivudine, GS-9131, dolutegravir, and cabotegravir.	*9131, dolutegravir, and cabotegravir.*	
77. The compound for use according to claim 70, wherein the compound is combined with tenofovir alafenamide, tenofovir alafenamide fumarate or tenofovir alafenamide hemifumarate. 98. The compound for use according to any one of claims 70 to 75, wherein the compound is combined with an additional therapeutic agent selected from the group consisting of abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate,	126. The compound for use of any one of claims 119 to 125, wherein the one, two, three, or four additional therapeutic agents are selected from abacavir sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide fumarate, and tenofovir alafenamide hemifumarate. *144. The use of any one of claims 137 to 142, wherein the one, two, three, or four additional therapeutic agents are selected from abacavir*	The claims are identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
tenofovir alafenamide, tenofovir alafenamide hemifumarate, emtricitabine, lamivudine, GS-9131, dolutegravir, and cabotegravir.	*sulfate, bictegravir, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, tenofovir alafenamide fumarate, and tenofovir alafenamide hemifumarate.*	
77. The compound for use according to claim 70, wherein the compound is combined with tenofovir alafenamide, tenofovir alafenamide fumarate or tenofovir alafenamide hemifumarate.	127. The compound for use of any one of claims 119 to 126, wherein the one, two, three, or four additional therapeutic agents are selected from tenofovir alafenamide, tenofovir alafenamide fumarate, and tenofovir alafenamide hemifumarate. *145. The use of any one of claims 137 to 144, wherein the one, two, three, or four additional therapeutic agents are selected from tenofovir alafenamide, tenofovir*	The claims are identical.

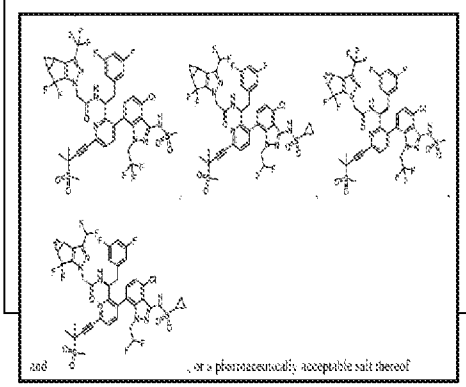
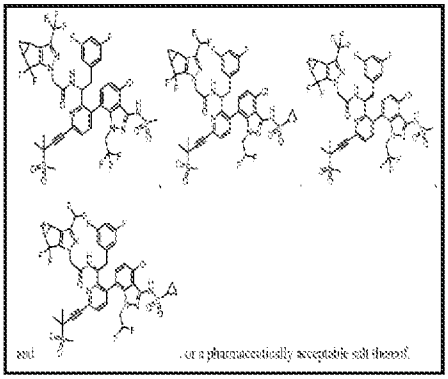
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	alafenamide fumarate, and tenofovir alafenamide hemifumarate.	
99. The compound for use according to any one of claims 70 to 75 and 98, wherein the compound is combined with an additional therapeutic agent selected from the group consisting of bictegravir, emtricitabine, and GS-9131.	128. The compound for use of any one of claims 119 to 124, wherein the one, two, three, or four additional therapeutic agents are selected from bictegravir, emtricitabine, and GS-9131.	The claims are identical.
90. The compound for use according to any one of claims 70 to 75, wherein the compound is combined with an additional therapeutic agent selected from the group consisting of: 	129. The compound for use of any one of claims 119 to 124, wherein the one, two, three, or four additional therapeutic agents are selected from: 	The claims are identical.

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	or a pharmaceutically acceptable salt thereof. *146. The use of any one of claims 137 to 142, wherein the one, two, three, or four additional therapeutic agents are selected from:*	

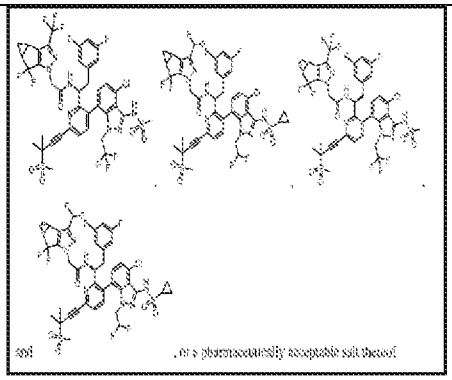
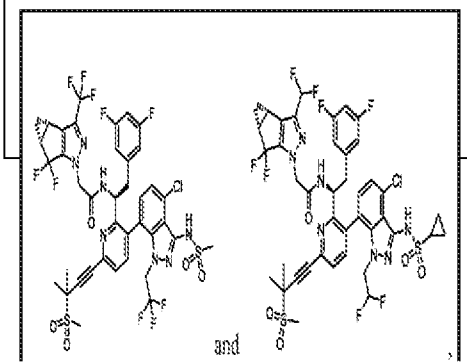
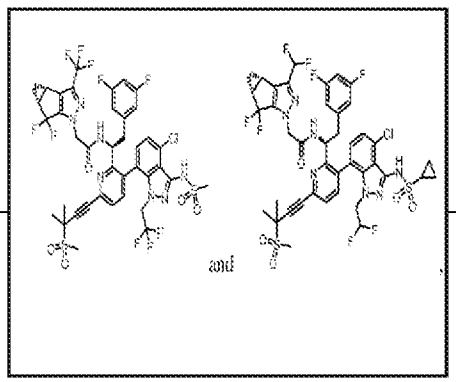
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	 *or a pharmaceutically acceptable salt thereof.*	
91. The compound for use according to any one of claims 70 to 75 and 90, wherein the compound is combined with an additional therapeutic agent selected from the group consisting of: 	130. The compound for use of any one of claims 119 to 124 and 129, wherein the one, two, three, or four additional therapeutic agents are selected from: 	The claims are identical.

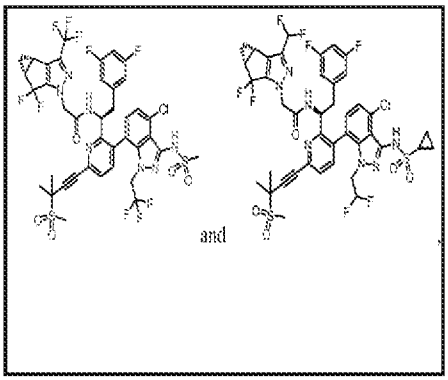
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
or a pharmaceutically acceptable salt thereof.	or a pharmaceutically acceptable salt thereof. *147. The use of any one of claims 137 to 142 and 146, wherein the one, two, three, or four additional therapeutic agents are selected from:*  and	

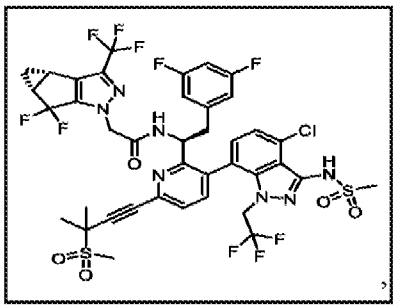
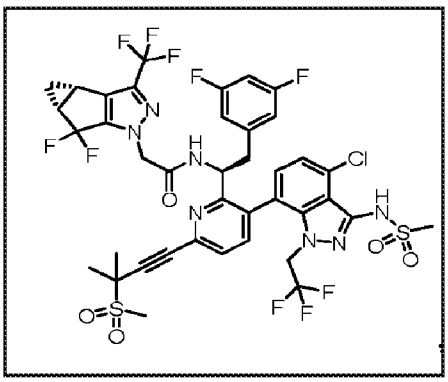
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	or a pharmaceutically acceptable salt thereof.	
92. The compound for use according to any one of claims 70 to 75, 90, and 91, wherein the compound is combined with: 	131. The compound for use of any one of claims 119 to 124 and 129 to 130, wherein the one, two, three, or four additional therapeutic agent is: 	The claims are identical.

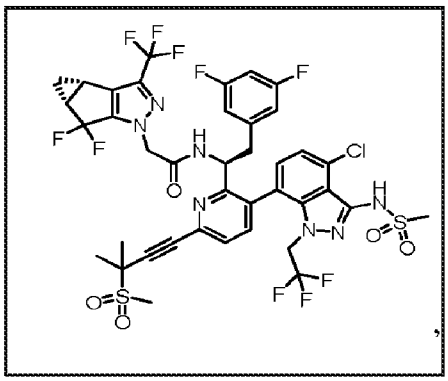
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
or a pharmaceutically acceptable salt thereof.	or a pharmaceutically acceptable salt thereof. *148. The use of any one of claims 137 to 142 and 146 to 147, wherein the one, two, three, or four additional therapeutic agent is:*  *or a pharmaceutically acceptable salt thereof.*	

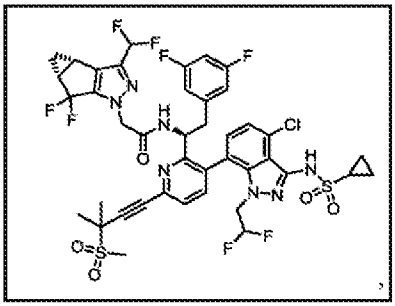
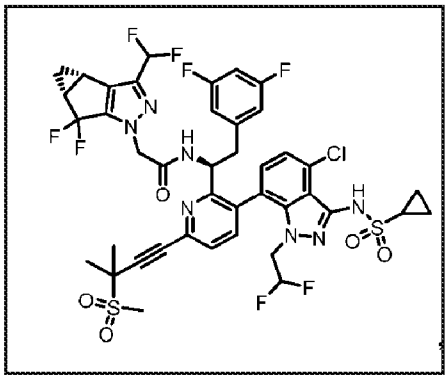
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 (WO'272)	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
93. The compound for use according to any one of claims 70 to 75, 90, and 91, wherein the compound is combined with:  or a pharmaceutically acceptable salt thereof.	132. The compound for use of any one of claims 119 to 124 and 129 to 130, wherein the one, two, three, or four additional therapeutic agent is:  or a pharmaceutically acceptable salt thereof.	The claims are identical.

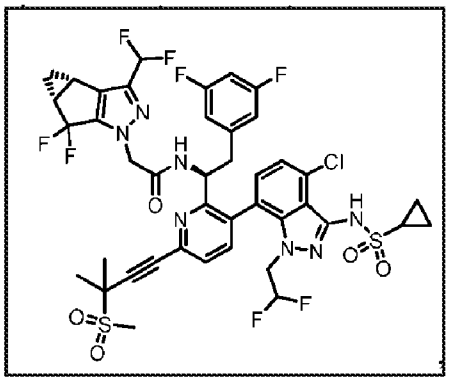
TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	149. The use of any one of claims 137 to 142 and 146 to 147, wherein the one, two, three, or four additional  *or a pharmaceutically acceptable salt thereof.*	

TABLE C: COMPARISON OF SECONDARY CLAIMS		
Prior art document, WO 2020/028272 **(WO'272)**	**Present Application, WO 2024/249517 (WO'517)**	**Comment**
	133. The compound for use of any one of claims 117 to 132, wherein the patient is a human. *150. The use of any one of claims 135 to 149, wherein the patient is a human.*	