PATENT COOPERATION TREATY

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THIRD PARTY OBSERVATION

(PCT Administrative Instructions Part 8)

Applicant's or agent's file reference 35648-0303WO1	
International application number PCT/US2023/030975	International filing date (day/month/year) 23 Aug 2023 (23/08/2023)
Applicant GILEAD SCIENCES, INC.	

Third party observation submitted by Anonymous	Observation submitted on behalf of
Date of submission(day/month/year) 24 Nov 2025 (24/11/2025)	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: 4
3. Further explanations:
   Uploaded copies of documents: 0

Citation # 1(Conference proceedings) (# uploaded documents: 2):

Author: Singh, R., et al.	Conference Title: 12th IAS Conference on HIV Science, 2023	Conference Date: 23 Jul 2023 (23/07/2023)
Conference Location: Brisbane, Australia	Title of article: Recommendations for missed oral lenacapavir loading doses using population-pharmacokinetics-based simulations	Place of publication:

Publisher:	Publication Date: 25 Jul 2023 (25/07/2023)	ISBN:
DOI:		

Most relevant passages or drawings: All pages	Relevant to Claims: 1-97

Brief explanation of relevance:

Singh et al., a team from Gilead Sciences, the Applicant of the present Application WO2025042394 (WO394), presented a poster titled “Recommendations for missed oral lenacapavir loading doses using population-pharmacokinetics-based simulations” at the “12th IAS Conference on HIV Science” (23–26 July 2023).

Singh et al. note the importance of oral lenacapavir (LEN) loading to achieve and maintain LEN concentrations above the therapeutic target ≥IQ4 [inhibitory quotient 4] and provide recommendations for people with HIV (PWH) who have missed oral loading doses; these recommendations were developed using a population pharmacokinetic (PopPK) simulation approach (Background; Objective).

They disclose (Methods; Results; Key Findings; Conclusions):
1. LEN is approved for the treatment of multidrug-resistant (MDR) HIV-1 infection in heavily treatment-experienced (HTE) adults, in combination with other antiretrovirals (ARVs)
2. Participants received LEN oral loading doses of 600 mg on Days 1 and 2 and 300 mg on Day 8, followed by 927 mg subcutaneous (SC) LEN on Day 15, with subsequent 927 mg LEN SC

maintenance doses given every 6 months from the Day 15 injection, as part of the Phase 2/3 CAPELLA regimen (NCT04150068); LEN was shown to be efficacious with a favorable safety profile (Fig 1)
3. Missing Day 2 and Day 8 loading doses resulted in LEN concentrations <IQ4
4. Considering the long terminal/apparent half-life of 10–12 days and 8–12 weeks following oral and SC LEN administration, respectively, when a loading dose is missed, the dosing window for oral LEN loading remains wide and forgiving
5. Missed dose scenarios of Day 2 and Day 8 oral loading doses (missed by <6 days and ≥6 days) were simulated to guide missed dose recommendations that maintain LEN concentrations above the therapeutic target (Fig 2)
6. Options for LEN oral loading doses to manage a missed oral loading dose (Table 1):
(i) if the Day 2 oral dose is missed by <6 days, a 600 mg oral dose should be taken as soon as possible, and 300 mg on Day 8;
(ii) if the Day 2 oral dose is missed by ≥ 6 days, a 600 mg oral dose should be taken as soon as possible, and a 300 mg on Day 15;
(iii) if the Day 8 oral dose is missed by <6 days, a 300 mg oral dose should be taken as soon as possible
(iv) If the Day 8 oral dose is missed by ≥6 days, a 300 mg oral dose should be taken on Day 15
7. In all the missed dose scenarios, LEN SC injection was given on Day 15
8. When a LEN SC dose was missed by >2 weeks then a restart of treatment was needed from Day 1; simulations for restart of treatment were conducted at steady state with dosing at 28 weeks after the last SC injection (Fig. 3).

WO394 claims: (i) methods of treating or preventing HIV using various dosing regimens, including (i.a) a 15-day initiation option regimen comprising an initiation dosage of 600 mg LEN orally on Days 1 and 2, 300 mg orally on Day 8, and 927 mg LEN SC on Day 15, followed by maintenance dosing of 927 mg LEN SC every 26 weeks with missed-dose alternatives for Days 2 and 8 missed oral doses; (i.b) a 2-day initiation option (ii) re-administration of initiation dosage before restarting the maintenance dosages, if a maintenance dosage is missed and >28 weeks have elapsed since the prior SC dose; (iii) method of treating HIV in HTE patients and patients infected with MDR HIV-1, event-driven administration, combination with additional therapeutic agents, etc. [Claims 1–97]. However, Singh et al. already disclose identical dosing regimen with 600 mg LEN on Days 1 and 2, 300 mg on Day 8, and 927 mg LEN SC on Day 15 followed by the maintenance regimen of 927 mg LEN SC administered every 6 months, as well as identical alternatives for the missed oral loading doses on Day 2 or 8, or the missed SC maintenance dose.

Further, WO2020018459 (WO459; Citation 4; LEN for treatment of HIV) and WO2021108544 (WO544; Citation 5; LEN for prevention of HIV) disclose the dosing ranges claimed in WO394 for LEN: A. WO544 also discloses (a) the composition of the film-coated tablet and of the SC solution comprising LEN sodium and other excipients, identical to that claimed in WO394, (b) the administration of additional therapeutic agents simultaneously (formulated as a unitary dosage form) or sequentially; B. WO459 further discloses a similar method of treating HIV-1 infection characterized by the identical MDR HIV-1 mutants (resistant to same ARVs) in HTE patients by administering similar tablet and SC solution formulations of LEN, either alone or in combination with other ARVs.

Thus, in light of Singh et al., read alone or with the Label for SUNLENCA (Citation 2; disclosing the 2-day initiation option for LEN), WO459 and/or WO544 (Citations 4 and 5 respectively), Claims 1 to 97 of the present Application, WO394, lack novelty (to the extent of overlap) and/or inventive step.

Citation # 2(Other) (# uploaded documents:1):

Identification of Document:	Publication Date:
Label – Highlights of prescribing information for SUNLENCA	Dec 2022 (12/2022)

Link to document:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215973s000lbl.pdf

DOI:

Most relevant passages or drawings:	Relevant to Claims:
pp.1–6, 13–16, 20–21, 25–26, 28–29, Fig. (p. 14), Tables 6, 7	1-97

Brief explanation of relevance:

The Label – prescribing information for SUNLENCA(R) [lenacapavir (LEN)] tablets for oral use, and injection for subcutaneous (SC) use states that, in combination with other antiretroviral(s) (ARVs), LEN is indicated for the treatment of HIV-1 infection in heavily treatment-experienced (HTE) adults with multidrug resistant (MDR) HIV-1 infection failing their current ARV regimen (pp.1 LHC, 2, 28).

The Label for SUNLENCA(R) discloses the following:

1. Recommended dosage includes initiation with one of the two initiation options, followed by once every 6-months maintenance dosing (pp.1–4, 28):

1.a) Initiation Option 1 comprises 927 mg by SC injection (2 x 1.5 mL injections of concentration 309 mg/mL) and 600 mg orally (2 x 300 mg tablets) on Day 1 and 600 mg orally (2 x 300 mg tablets) on Day 2; or

1.b) Initiation Option 2 comprises 600 mg orally (2 x 300 mg tablets) each on Days 1 and 2, 300 mg orally (1 x 300 mg tablets) on Day 8 and 927 mg by SC injection (2 x 1.5 mL injections) on Day 15; and

1.c) Maintenance dose comprises 927 mg by SC injection (2 x 1.5 mL injections) every 6 months (26 weeks) from the date of the last injection or plus or minus 2 weeks.

2. Maintenance dosing by injection is required every 6 months, because missed doses or non-adherence to injections could lead to loss of virologic response and development of resistance. If a maintenance dose is missed, i.e., more than 28 weeks have elapsed since the last injection, it is recommended to restart initiation dosage (Option 1/2) from Day 1 (pp.1 LHC, 3, 5, 26, 28–29).

3. If LEN is discontinued, initiate an alternative, fully suppressive ARV regimen, where possible, no later than 28 weeks after the final injection of LEN, to minimize risk of viral resistance. If virologic failure occurs, switch to the alternative regimen [as stated above] if possible (pp.1 RHC, 5).

4. Each film-coated tablet contains 300 mg of LEN (present as 306.8 mg of LEN sodium), and copovidone, croscarmellose sodium, magnesium stearate, mannitol, microcrystalline cellulose, and poloxamer 407 as the inactive ingredients. Each SC injection in the form of single-dose vial contains 463.5 mg/1.5 mL (309 mg/mL) of LEN (present as 473.1 mg/1.5 mL of LEN sodium) and 896.3 mg of polyethylene glycol (PEG) 300 (as solvent) and water for injection, and a pH range of 9.0–10.2 (pp.4, 13–14, 25, 29, Fig. of LEN Na on p.14)

5. The PK properties of oral and SC were determined, and the estimated LEN exposures are comparable between the two recommended dosing regimens (pp.15–16; Tables 6, 7)

6. Oral LEN and SC LEN shows an elimination half-life of 10–12 days and 8-12 weeks, respectively (p.15, Table 6)

7. Clinical assessment of LEN (i) in HTE adults (with documented resistance to at least two ARV medications from each of at least 3 of the 4 ARV classes—NRTI, NNRTI, PI and INSTI; emergent resistance substitutions, e.g., M184I/V, K65R, etc.) in Phase 2/3 CAPELLA (NCT04150068) trial, comprised administering oral loading doses (600 mg on Days 1 and 2, 300 mg on Day 8) followed by SC doses (927 mg every 6 months starting on Day 15); and (ii) in treatment-naïve adults in Phase 2 CALIBRATE trial (pp.6–8, 14–16, 20–25).

The present Application, WO2025042394 (WO'394), claims method of treating or preventing HIV comprising administering Formula 1(a) or 1(b) (LEN) as sodium salt, comprising an initiation dosage in the 1st time period, either for 2 days (SC 927 mg, oral 600 mg on Day 1; oral 600 mg on Day 2), or for 15 days (oral 600 mg on Days 1 and 2, oral 300 mg on Day 8; SC 927 mg on Day 15); and maintenance dosage of 927 mg every 6 months in the 2nd time period. WO'394 also claims the alternative regimen in case of missed oral initiation dosage (on Day 2 or Day 8) or missed maintenance dosage (if more than 28 weeks have elapsed. WO'394 also claims the composition of the LEN tablet and SC solution. Tablet is prepared by spray-dried technique. Administered as a monotherapy as PreP, PEP, or in HTE patients; combination therapy too [Claims

1–97].

However, the Label for SUNLENCA already discloses the identical dosing regimen comprising initiation dosage (option 1 or 2), the maintenance dosage, and missed maintenance dose for more than 28 weeks; in HTE patients infected with MDR-HIV, and discloses the excipients of the oral and SC injection, as claimed in WO'394.
Further,
(i) Singh et al., and the Sunlenca EPAR-Product information [Citations 1 and 3, respectively] disclose alternative dosing regimen in case of missed oral initiation dosage (on Day 2 or Day 8)
(ii) WO2020018459 [Citation 4] claims LEN for treatment of HIV, the composition of oral and SC LEN, etc.
(iii) WO2021108544 [Citation 5] disclose LEN for PrEP of HIV, event-driven administration, etc.

Thus, all the claims of WO'394 lack inventive step.

Citation # 3(Other) (# uploaded documents:1):

Identification of Document:	Publication Date:
Sunlenca : EPAR – Product Information	25 Aug 2022 (25/08/2022)
Link to document: https://web.archive.org/web/20230220175400/https://www.ema.europa.eu/en/documents/product-information/sunlenca-epar-product-information_en.pdf	
DOI:	
Most relevant passages or drawings: pp. 2–3, 16, 18–19, 22, 26–27, 32, 48, 57; Tables 1 and 2	Relevant to Claims: 1, 2, 8–23, 25–28, 30–97

Brief explanation of relevance:

As of February 2023, the "Sunlenca : EPAR – Product Information" (Sunlenca Product Information) [EPAR = European Public Assessment Report], discloses the following about lenacapavir (LEN), an HIV capsid inhibitor (pp.48, 57), including the dosing regimen to be followed in case of missed doses:

A. Recommended treatment regimen: initiation and maintenance dosing schedule (pp.2–3, 18–19; Table 1):

A.1. Initiation dosage
Day 1: 600 mg orally (2 x 300 mg tablets)
Day 2: 600 mg orally (2 x 300 mg tablets)
Day 8: 300 mg orally (1 x 300 mg tablet)
Day 15: 927 mg subcutaneous (SC) injection (2 x 1.5 mL injections; solution for injection)

A.2. Maintenance dosage
Once every 6 months (26 weeks from date of last injection) +/- 2 weeks: 927 mg SC injection (2 x 1.5 mL injections)

B. Regimen in case of missed oral initiation dose (p.19):
If the Day 2 (600 mg) oral dose is missed by:
- less than 6 days, patient to take 600 mg as soon as possible, and 300 mg by Day 8.
- 6 days or more, patient to take 600 mg as soon as possible, and 300 mg on Day 15.
If the Day 8 (300 mg) oral dose is missed by:
- less than 6 days, patient to take 300 mg as soon as possible.
- 6 days or more, patient to take 300 mg on Day 15.
Regardless of when the Day 2 or Day 8 oral dose is being taken, SC injection to be administered on Day 15.

C. In case of missed maintenance dose, if more than 28 weeks have elapsed since the last SC injection, the regimen is to be restarted from Day 1 (p.3).

D. Composition of the core of each film-coated tablet: LEN sodium equivalent to 300 mg of LEN and excipients: mannitol, microcrystalline cellulose, croscarmellose sodium, copovidone, magnesium stearate and poloxamer (pp.18, 32)

E. Composition of each single-dose vial: LEN sodium equivalent to 463.5 mg of LEN in 1.5 mL and excipients: macrogol and water for injections (pp.2, 16)

F. The tablet, in combination with other antiretroviral(s) (ARVs), is indicated for the treatment of adults with multidrug resistant (MDR) HIV-1 infection, for oral loading prior to administration of long-acting LEN injection (p.18).

G. Synergistic antiviral effects were observed in a study of LEN in combination with representatives from main classes of ARV agents (nucleoside reverse transcriptase inhibitors [NRTIs], non-nucleoside reverse transcriptase inhibitors [NNRTIs], integrase strand-transfer inhibitors [INSTIs], and protease inhibitors [PIs]) (p.26; also p.22, Table 2).

H. LEN remained fully active “against a broad spectrum of HIV-1 site-directed mutants and patient-derived HIV-1 isolates with resistance to” NRTIs, NNRTIs, INSTIs, PIs as well as maturation inhibitors and those resistant to entry inhibitors, “thereby demonstrating a non-overlapping resistance profile” (p.27).

The present Application, WO2025042394 (WO394), claims method to treat or prevent (as pre- and /or post-exposure prophylaxis) HIV with either a 2-day or a 15-day initiation regimen option of LEN (Formula Ia, Ib; sodium salt). The 15-day initiation dosage regimen comprises: oral LEN (tablet) on Days 1, 2 and 8 followed by SC LEN (solution) on Day 15, with details of the schedule in case of missed oral dose during the initiation period; and a maintenance regimen (927 mg; 2 x 1.5 mL injections) of SC LEN every 26 weeks, which commences 26 weeks after final administration of the initiation dosage; restarting regimen in case of missed maintenance dose if more than 28 weeks have elapsed since the prior SC dose (Claims 1, 2, 8–23, 25–28, 30–60, 96–97). WO394 further claims such treatment as monotherapy or as a combination of ARVs (Claims 48, 88–95); the patient may be a heavily treatment experienced patient with HIV-1 mutant resistance to one or more ARVs or with MDR HIV-1, or has failed previous treatment regimen (Claims 61–87).

However, the Sunlenca Product Information already discloses (i) the same 15-day initiation regimen, including the schedule in case of missed oral doses, followed by the maintenance regimen of LEN, for treatment of HIV, as has been claimed in the present Application, WO394; and (ii) the effectiveness of LEN in combination with other ARVs as well as its activity against HIV mutant variants.

While the present Application, WO394, claims a dosing range, it may be noted that these ranges include the doses specifically disclosed by the Sunlenca Product Information. These ranges are also disclosed in WO2020018459 (WO459; LEN for treatment of HIV) and WO2021108544 (WO544; LEN for HIV pre- and post-exposure prophylaxis) (Citations 4 and 5 respectively).

In light of Sunlenca Product Information, read alone or with WO459 and / or WO544 (Citations 4 and 5 respectively), Claims 1, 2, 8 to 23, 25 to 28 and 30 to 97 lack novelty (to the extent of overlap) and/or inventive step.

Citation # 4 (Patent/utility model) (# uploaded documents: 0):

Country code:	Publication number:	Document kind code:
WO	2020/018459	A1

Patent Applicant/Patent Owner:	Title of invention:
Gilead Sciences, Inc.	Capsid inhibitors for the treatment of HIV

Link to document:
https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2020018459

Publication Date:	Filing Date:	Priority Date:
23 Jan 2020 (23/01/2020)	15 Jul 2019 (15/07/2019)	16 Jul 2018 (16/07/2018)

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

Most relevant passages or drawings:	Relevant to Claims:
Abstract; pp.1–8, 11–13, 15–34, 36–47, 58, 79, 97–114, 117–151, 185; Ex.3S; Table T, Table 15; Claim 1–27, 31–41, 43–50, 56–86, 88–90, 102–107	1-97

Brief explanation of relevance:

WO2020018459 (WO459), by the Applicant of the present Application, WO2025042394 (WO394), discloses methods of treating HIV infection in heavily treatment-experienced (HTE) patients with multidrug resistant (MDR) HIV infection by administering Compound Ia (i.e., lenacapavir; LEN) or its salt (Abstract; pp.1–2). [It may be noted that Compound Ia of WO459 is identical to Compound Ib claimed in WO394].

WO459 discloses and/or claims a method of treating HIV infection wherein (Claim 1; pp.3–8, 11–13, 15–34, 36–47, 58, 79, 97–114):

1. LEN or its sodium salt (LEN Na) is administered orally (one/more tablets), subcutaneously (e.g. solution; at about 50–500 mg/mL; 300 mg/mL), etc (Claims 26–27, 31–41; pp.16, 58, 79, 97, 114)
2. LEN or LEN Na salt, is administered once daily, or once every 1, 2, 24, 48, etc. week/s, e.g. orally once every week, subcutaneously (SC) once every 6 months (pp.118–119); dosage amount is about 1–1000 mg (e.g., 300, 600, 900, 950 mg); weekly dose of 300 mg (Claims 46–50; pp.117–129)
3. Solution administered comprises [values in percent w/w] 10–40 water, 35–75 PEG300 and 5–35 LEN Na (Claims 88–90)
4. Tablet is prepared from spray-dried dispersion technology, and comprises [values in percent w /w] 5–45 (e.g. 300 mg) LEN Na, 1–10 copovidone, 0.01–10 poloxamer 407, 5–45 microcrystalline cellulose, 15–70 mannitol, 1–30 croscarmellose sodium, 0.01–10 magnesium stearate; the tablet with an outer film coat, providing 1–8 percent weight gain based on the uncoated tablet (Claims 102–107; p.185; Ex.3S; Table T)
5. HIV-1 infection is characterized by HIV-1 mutant resistant to 1/2/3 or more antiretroviral medications (ARV) (Claims 2–4)
6. HIV-1 mutant is resistant to a (i) protease inhibitor (PI), mutant selected from I50V, I84V/L90M, G48V/V82A/L90M, and G48V/V82S; (ii) nucleos(t)ide reverse transcriptase inhibitor (NRTI), mutant selected from K65R, MI 84V, and 6TAMs; (iii) non-nucleos(t)ide reverse transcriptase inhibitor (NNRTI), mutant selected from K103N, Y181C, Y188L, L100I/K103N, and K103N/Y181C; or an (iv) integrase strand transfer inhibitor (INSTI), mutant selected from Y143R, E138K/Q148K, G140S /Q148R, E92Q/N155H, N155H/Q148R, and R263K/M50I (Claims 5–9)
7. The patient is infected with HIV-1 resistant to at least one ARV or with MDR HIV-1 resistant to at least one ARV from each of 2/3 different ARV classes, i.e. NRTI (e.g., emtricitabine, 3TC, etc.), NNRTI (e.g., rilpivirine, etc.), PI (e.g., lopinavir, darunavir, etc.), INSTI (e.g., cabotegravir, bictegravir, etc.) (Claims 10–17)
8. The patient had been previously treated with at least one ARV medication for at least 3, 6, 9 or 12 months (Claims 18–22)
9. The patient (a) has failed a prior HIV treatment regimen; (b) is failing an HIV treatment regimen at the time of beginning administration of LEN or its salt; or (c) failed the previous treatment regimen and LEN administration results in a reduction in HIV viral load; the regimen comprises at least one ARV medication from each of 2/3 different ARV classes (Claims 22–25, 56–65, 74–86)
10. The patient is concurrently treated with at least one additional ARV, or one/more additional therapeutic agents in combination (simultaneous/sequential) with LEN; method for treating /preventing HIV infection therewith; LEN formulated with one/more other compounds (Claims 43–45, 66–73; pp.129–151; activity in combination with other ARVs: p.189, Table 15).

The present Application, WO394 claims method of treating/preventing HIV (i) with a dosing

regimen comprising initiation and maintenance dosage and alternatives to the missed maintenance or oral loading (Day 2 or 8) dosage, wherein LEN (Compound Ia/Ib), or LEN Na is administered orally (film-coated tablet) and SC (solution), the dosage forms having specific composition; (ii) in HTE patients infected with MDR HIV-1, wherein the specific HIV-1 mutants are resistant to multiple drugs of different ARV classes (NRTI, NNRTI, PI, INSTI), the patient is failing the current ARV regimen, and administration of LEN decreases viral load; (iii) event-driven administration; etc [Claims 1–97].

However, (a) WO459 already discloses a similar method of treating HIV-1 infection characterized by the identical MDR HIV-1 mutants (resistant to identical ARVs), in HTE patients, previously treated and failing their current treatment regimen, and showing decrease in viral load due to LEN, by administering similar tablet and SC solution formulations comprising LEN Na and identical excipients as that claimed in WO394; (b) WO2021108544 [Citation 5] discloses event-driven administration of LEN, for preventing HIV-1 infection; (c) Sunlenca EPAR- Product Information [Citation 3] discloses a 15-day dosing regimen and alternatives to missed doses, identical to that claimed in WO394.

Thus, in light of the above, all Claims 1–97 of WO394 lack, inventive step.

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

Country code:	Publication number:	Document kind code:
WO	2021/108544	A1

Patent Applicant/Patent Owner:	Title of invention:
Gilead Sciences, Inc.	Capsid inhibitors for the prevention of HIV

Link to document:
https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2021108544

Publication Date:	Filing Date:	Priority Date:
03 Jun 2021 (03/06/2021)	25 Nov 2020 (25/11/2020)	26 Nov 2019 (26/11/2019)

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

Most relevant passages or drawings:	Relevant to Claims:
Abstract; pp. 1–6, 8–27, 36, 37, 38–40, 41-50, 113, 115, 117-127, 128–140; Claims 1–6, 15, 21, 25–27, 31–81, 84–92; Figs 1, 2, 3	1-97

Brief explanation of relevance:

WO2021108544 (WO544), an earlier application by the Applicant of the present Application, WO2025042394 (WO394), relates to methods of preventing HIV or reducing the risk of HIV by administering a therapeutically effective amount of a compound of Formula (Ia) (i.e., lenacapavir; LEN) or its pharmaceutically acceptable sodium salt (LEN Na) on a daily or intermittent dosing regimen (e.g., every 4, 28 or 48 weeks), optionally in combination with additional therapeutic agents (pp.1–4, 23–24, 36; Abstract). [It may be noted that Compound Ia of WO544 is identical to Compound Ib claimed in WO394].

WO544 discloses and/or claims a method of preventing HIV–1 or 2 by administering therapeutically effective amount of LEN Na (pp.6, 127; Claims 1, 84–88, 91–92), wherein:
1. LEN Na is administered orally as a tablet (prepared by spray-dried dispersion) comprising about 300 mg LEN (pp.25–26, 38, 39, 113, 115; Claims 2–4, 11–12, 14, 25, 27).
2. The tablet comprises 5–45 (particularly 15–25) w/w percent of LEN Na, 1–10 (particularly 3–6) w /w percent of copovidone, 0.01–10 (particularly 0.5–3) w/w percent of poloxamer 407, 5–45 (particularly 18–30) w/w percent of microcrystalline cellulose, 15–70 (particularly 40–50) w/w percent of mannitol, 1–30 (particularly 6–10) w/w percent of croscarmellose sodium and 0.01–10 (particularly 1–3) w/w percent of magnesium stearate (pp 27; Claims 24–28).
6. LEN Na is administered with up to three additional agents, either simultaneously or sequentially, as a unitary dosage form. Additional agents may include HIV protease, reverse transcriptase, integrase, gp41, CXCR4, gp120, CCR5, or capsid inhibitors and broadly neutralizing antibodies, bispecific antibodies, or HIV vaccines (pp.1, 3, 37, 128–130, 135–140; Claims 31–36).
7. Additional therapeutic agent is selected from tenofovir alafenamide, tenofovir disoproxil, tenofovir alafenamide hemifumarate, bictegravir or pharmaceutically acceptable salt thereof (pp.131–132; Claims 37–48, 80–81).
8. Event-driven administration of LEN for pre-exposure (PrEP) and/or post-exposure (PEP) prophylaxis; PrEP comprises continuous administration, wherein LEN Na is administered before exposure to HIV at about 14, 10, 7, 5 days or 72 to 1 hour prior to exposure, during the period of exposure (once every 2 months or months) and/or 1 hour to 14 days after the final exposure to HIV (pp.6–22; Claims 51–78; Figs. 1, 2, 3).

The present WO2025042394 (WO394), claims (i) a method for treating or preventing (PrEP/PEP) HIV infection using a compound of Formula Ia or its sodium salt (injectable solution or oral tablets) (ii) an **initiation phase (oral 300-600 mg and SC 927 mg with specific dosing scheduled on Days 1, 2, 8 and 15)** followed by **maintenance dosing (SC administration every 26 week,** with re-initiation required if more than 28 weeks elapse after last maintenance dose**)** (iii) alternative regimen for missed oral loading dose (Day 2 or 8) based on the delay period (iv) method for treating **HIV-1**, including MDR HIV and HTE **patients** (v) LEN **as monotherapy or in combination** with other antiretroviral agents. (Claims 1–97).

However, WO544 already discloses (a) methods for preventing HIV infection or reducing the risk of acquiring HIV by administering LEN Na either orally as a tablet or SC injection in a specific dosing regimen; wherein the composition of the film-coated tablet (prepared from spray-dried dispersion technology) and that of the SC solution, comprising LEN Na and other excipients, is identical to that claimed in WO394; (b) administration of additional therapeutic agents simultaneously or sequentially, formulated as a unitary dosage form; (c)administration may be event-driven for PrEP and/or PEP, with LEN given continuously or at defined time points before (at about 14, 10, 7, 5 days or 72 to 1 hour before), during and/or after HIV exposure.

Further:
1. identical dosing regimen (SC and oral) comprising initiation and maintenance dosage and the alternatives for missed doses, as that claimed in WO394, is already disclosed in Singh et al., Sunlenca EPAR-product information and Label – Prescribing Information for SUNLENCA [Citations 1, 3 and 2, respectively].
2. WO2020018459 [Citation 4] discloses LEN for treatment of HIV in HTE patients.

Thus, in light of the above Claims 1–97 of WO394 lack inventive step.