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08th April, 2021

The Controller of Patents,
Indian Patent Office,
Intellectual Property Office Building,
Plot No 32, Sector -14, Dwarka
New Delhi

Re: Pre-grant Opposition against Indian Patent Application No. 201917006277 filed on 18th February, 2019 u/s 25(1) filed by The Delhi Network of positive people (DNP+)
Applicant: GILEAD SCIENCES, INC.
Title: THERAPEUTIC COMPOUNDS USEFUL FOR THE PROPHYLACTIC OR THERAPEUTIC TREATMENT OF AN HIV VIRUS INFECTION
Opponent: The Delhi Network of positive people (DNP+)

Respected Sir,

We are filing this Pre-Grant Representation/Opposition U/S 25 (1) of the Patents Act, 1970 and Rule 55 of the Patent Rules, 2003 in Form 7A.

The Learned Controller is requested to take the documents on record and proceed further in the matter and keep the Petitioner advised of each and every step taken in the matter.

We crave the leave of the Learned Controller to submit additional documents or evidence or if necessary to support any of the averments in the representation as may be necessitated in the proceeding.

Lastly, we request the Learned Controller to grant an opportunity of being heard before the above representation is finally decided.

Yours Sincerely,

RAJESHWARI H. IN/PA-358
AGENT FOR THE OPPONENT
RAJESHWARI & ASSOCIATES

Encl.: As stated

C.C.: K & S PARTNERS

BEFORE THE CONTROLLER OF PATENTS, THE PATENT OFFICE, NEW DELHI

In the matter of Section 25(1) of The Patents Act,1970 as amended by The Patents (Amendment) Act 2005;

And

In the matter of Rule 55 of The Patents Rules 2003 as amended by the Patent (Amendment) Rules, 2006

And

IN THE MATTER of Indian Patent Application No. 201917006277 filed on 18/02/2019 by GILEAD SCIENCES, INC.

REPRESENTATION BY:

THE DELHI NETWORK OF POSITIVE PEOPLE .....OPPONENT

VS.

GILEAD SCIENCES, INC. .....APPLICANT

REPRESENTATION BY WAY OF OPPOSITION U/S 25(1)

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4.	**D1:** Copy of WO2014134566	49-475
5.	**D2:** Copy of WO2013006738	476-1138
6.	**D3:** Copy of WO2016033243	1139-1391
7.	**D4:** Copy of article Gerben van 't Klooster 1, Eva Hoeben, Herman Borghys, Adriana Looszova, Marie-Paule Bouche, Frans van Velsen, LievenBaert; Pharmacokinetics and disposition of rilpivirine (TMC278) nanosuspension as a	1392-1400

	long-acting injectable antiretroviral formulation; Antimicrob Agents Chemother. 2010 May;54(5):2042-50. doi: 10.1128/AAC.01529-09. Epub 2010 Feb 16.	
8.	**D5:** Copy of article Katia P. Seremetaa,b, Diego A. Chiappettaa,b, Alejandro Sosnika,b; Poly(-caprolactone), Eudragit® RS 100 and poly(-caprolactone)/Eudragit® RS 100 blend submicron particles for the sustained release of the antiretroviral efavirenz; Colloids and Surfaces B: Biointerfaces Volume 102, 1 February 2013, Pages 441-449	1401-1409
9.	**D6:** Copy of article William R Spreen 1, David A Margolis, John C Pottage Jr; Long-acting injectable antiretrovirals for HIV treatment and prevention; CurrOpin HIV AIDS. 2013 Nov;8(6):565-71	1410-1416
10.	**D7:** Copy of article Neha Jindal S.K. Mehta; Nevirapine loaded Poloxamer 407/Pluronic P123 mixed micelles: Optimization of formulation and in vitro evaluation; Colloids and Surfaces B: Biointerfaces Volume 129, 1 May 2015, Pages 100-106	1417-1423
11.	**D8:** Copy of article Landovitz RJ, Kofron R, McCauley M. ; The Promise and Pitfalls of Long Acting Injectable Agents for HIV Prevention; CurrOpin HIV AIDS 2016;11(1):122-128	1424-1434
12.	**D9:** Copy of WO2016046786	1435-1482
13.	Power of Attorney	

Dated this day 08th of April, 2021

RAJESHWARI H IN/PA - 0358
AGENT FOR THE OPPONENT
OF RAJESHWARI AND ASSOCIATES

To,
The Controller of Patents
The Patent Office, Delhi

FORM 7A
THE PATENTS ACT,
1970 (39 OF 1970)
AND
THE PATENTS RULES, 2003
REPRESENTATION FOR OPPOSITION TO GRANT OF PATENT
[See Rule 55]

We, **THE DELHI NETWORK OF POSITIVE PEOPLE**, having address at A1-5, House No. 141 Gali No. 3, IGNOU Main Road, Neb Saral, New Delhi - 110068; India hereby give representation by way of opposition to the grant of patent in respect of application No: **201917006277 filed on 18/02/2019** made by **GILEAD SCIENCES, INC.** on the grounds:

i. Section 25(1)(b)(i)- invention so far as claimed in any claim of the complete specification has been published
ii. Section 25(1)(d)- invention so far as claimed in any claim of the complete specification was publicly known or publicly used in India
iii. Section 25(1)(e) – the invention so far as claimed in any claim of the complete specification is obvious and clearly does not involve any inventive step
iv. Section 25(1)(f) - Subject of any claim of the complete specification is not an invention
v. Section 25(1)(g)-Complete specification does not sufficiently and clearly describe the invention

(**Detailed grounds are set out in the Opposition as attached**)

My address in India is:

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Dated, this 08th day of April, 2021

RAJESHWARI H IN/PA - 0358
AGENT FOR THE OPPONENT
OF RAJESHWARI AND ASSOCIATES

To
The Controller of Patents,
The Patent Office, Delhi

BEFORE THE CONTROLLER OF PATENTS,THE PATENT OFFICE, DELHI

IN THE MATTER OF:

The Patents Act, 1970 as amended by the Patents (Amendment) Act 2005, and The Patents Rules, 2003, as amended by The Patents (Amendment) Rules, 2006

AND

IN THE MATTER OF:

An opposition by way of representation under Section 25(1) of The Patents, 1970, as amended by the Patents (Amendment) Act, 2005 read with Rule 55 of The Patents Rules, 2003, as amended by The Patents (Amendment) Rules, 2006 to the Indian National Phase Application No. 201917006277 filed on 18/02/2019 by **GILEAD SCIENCES, INC.**

IN THE MATTER OF:

THE DELHI NETWORK OF POSITIVE PEOPLE .....OPPONENT

VS.

GILEAD SCIENCES, INC. .....APPLICANT

REPRESENTATION BY WAY OF OPPOSITION U/S 25(1)
OPPONENT'S BACKGROUND &*LOCUS STANDI*

1. The Opponent, **THE DELHI NETWORK OF POSITIVE PEOPLE**, is a community based non-profit organisation representing the needs of people living with HIV/AIDS ("PLHAs") and Hepatitis C (HCV), and is registered as a Trust under Registration No. 8525, Additional Book No. 1423/1-23 IV Sub

Registrar, New Delhi, with its registered address at Flat no. A1-5, Property 141 Gali No. 3, Harijan Colony, Neb Sarai, New Delhi, 110068.

2. The Opponent is a PLHIV (People Living with HIV) network working extensively in the area of access to medicines. The Opponent's work includes but is not limited to service delivery, treatment literacy and community empowerment. The main focus and emphasis is advocating for access to medicines as they believe every individual should get treatment and no one should suffer and die due to lack of medicines. Of main concern to the Opponent, is the impact of product patent protection on access to effective and affordable tuberculosis medicines for people not just in India but across the developing world.

3. Cognisant of public health concerns, Parliament introduced certain provisions, while passing the Patents (Amendments) Act, 2005 to amend the Patents Act, 1970 (hereinafter referred to as the "Patents Act"), to ensure that patents are granted only for genuine inventions. The statute seeks to prevent "ever-greening", i.e. creation or extension of monopolies through patent terms by obtaining patents for minor or routine modifications.

4. The Opponents firmly believe that a proper application of the patentability standards set out in Section 3of the Patents Act, as well as those embodied in Section 2(1)(j) and Section 2(1)(j)(a) of the Patents Act, in a manner that fully carries out the objectives of the Amending Act, will result in the rejection of the present application in its entirety. The Opponents, therefore, humbly request the Hon'ble Patent Controller to scrutinise the present application with special care, as its decision will determine whether millions of people will have access to affordable life-saving treatment.

5. As per S.25(1), a pre-grant opposition can be instituted by any person as long as an Application is still under prosecution. The present Application has not matured into a patent as of the date of filing of this pre-grant

representation. Hence, the present pre-grant opposition being filed by opponent is validly filed and is not time barred. A copy of the complete specification with claims (latest set of12 claims from March 2021) and downloaded from IPASS is attached as **Annexure 1**.

PRESENT APPLICATION

6. The Opponent has reviewed the file available at the IPASS system of the Indian Patent Office in respect of present Application and notes that this Indian application was filed at the Patent Office, New Delhi. According to the information and documents available therein, following are the relevant details:

APPLICATION NUMBER	201917006277
PRIORITY DATE	19/Aug/2016
PCT DETAILS	PCT/US2017/047416; Published as WO2018035359
PCT INTERNATIONAL FILING DATE	17/Aug/2017
APPLICANT NAME	**GILEAD SCIENCES, INC.**
TITLE OF INVENTION	THERAPEUTIC COMPOUNDS USEFUL FOR THE PROPHYLACTIC OR THERAPEUTIC TREATMENT OF AN HIV VIRUS INFECTION
DATE OF FILING	18/Feb/2019
REQUEST FOR EXAMINATION DATE	18/Feb/2019
PUBLICATION DATE (U/S 11A)	03/May/2019
FIRST EXAMINATION	26/Nov/2019

REPORT DATE	
REPLY TO FER DATE	18/May/2020
SER DETAILS	05/Jan/2021 Hearing held on 08/Mar/2021
REPLY TO SER DATE	Reply filed on 10/Mar/2021

PRESENT SPECIFICATION& CLAIMS

7. The present Specification runs into approx. into 115+ pages and was filed with 46 claims. After the FER, the Applicant responded and amended these to 15 claims (May 2020). After the hearing of March 2021, the Applicant filed a response and amended the 15 claims to the present set of 12 claims.These 12 claims are divided amongst following groups:
   i) Current claim 1 is an independent claim for a specific compound (Ia), with claim 2being dependent on claim 1.
   ii) Claim 3 is an independent claim for a specific compound (IIa), with claim 4 being dependent on claim 4.
   iii) Claim 5 is for a parenteral formulation having the compound from earlier claims +poloxamer.
   iv) Claim 6 is for an intermediate compound.
   [Preparation of compound 12 is used in the preparation of compound 24 i.e.Lenacapavir refer example 5 at page no. 86. A preparation of compound 32 is used in the preparation of compound 38 (IIb), refer example 8 at page no.94]
   v) Claims 7-8 are dependent on formulation claim 5.
   vi) Claim 9 claims a parenteral composition with multiple components. Claim 10-11 are dependent on claim 9.
   vii) Claim 12 covers a parenteral formulation of previous claims, where the compound is in the form of a sodium salt.

EXAMINATION REPORT(S) & APPLICANT RESPONSE:

8. The Patent Office issued the First Examination Report (FER) in Nov 2019 on the original 46 claims with the following objections:
    - Lack of inventive step for all 46 claims;
    - S.3(d) & S3(e) objections for all 46 claims;
    - S.10 objections for all 46 claims.

9. The Controller cited following 3 documents:
    D1: US201403164 [filed in India as 7440/DELNP/2014]
    D2: WO2013006738
    D3: WO2013006792

10. The Applicant filed a response to the FER in May 2020. While responding to the inventive step objection against D1 of the FER, the Applicant stated that '*To arrive at the claimed compounds, at least the following selections from D1 must be made*' and asserted that presently claimed compounds (Ia – compound 24 of present Specification) and (IIa – compound 38 of present Specification) exhibit EC_{50} values of 0.185 nM and 0.399 nM, respectively, as compared with EC_{50} values of 1.715 nM and 2.991 nM for Compounds A and B of D1.

11. In Jan 2021, Controller issued a hearing notice for these 15 claims,whereinhemaintained the inventive step and 3(d) objection. Controller also issued multiple objections to new claim 15 (S.59/ S.10/ S.2(1)(j). A hearing was conducted on 08/Mar/2021 and thereafter, Applicant filed a written reply on 10/Mar/2021 and also amended the 15 claims to 12 claims, while deleting the earlier added claim 15 and repeating its earlier arguments.

GENERAL BACKGROUND ON HIV, INDIA DETAILS AND LENACAPAVIR

12. HIV (Human Immunodeficiency Virus) is a virus that attacks the body's immune system. If HIV is not treated, it can lead to AIDS (Acquired Immuno Deficiency Syndrome). Once people get HIV, they have it for life[1]. There is currently no effective cure and as treatment is not curative; consequently, patients must be treated for their entire lives. To address the issue of multidrug resistance in PLHIVs a long acting, safer and effective alternative treatment for PLHIV's having higher suppression of the viral load is required. There were an estimated 23.48 lakh (17.98 lakh – 30.98 lakh) PLHIV in 2019[2] in India.

13. The HIV infection is treated by using anti-retro viral treatment. Following are major classes of ARTs currently being used for treating HIV/ AIDS:
    - Nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs)
    - Nonnucleoside reverse transcriptase inhibitors (NNRTIs)
    - Protease inhibitors (PIs)
    - Integrase inhibitors (IIs)
    - Fusion inhibitors (FIs)
    - Chemokine receptor antagonists (CRAs)
    - gp120 Attachment Inhibitor
    - CCR5 Antagonist

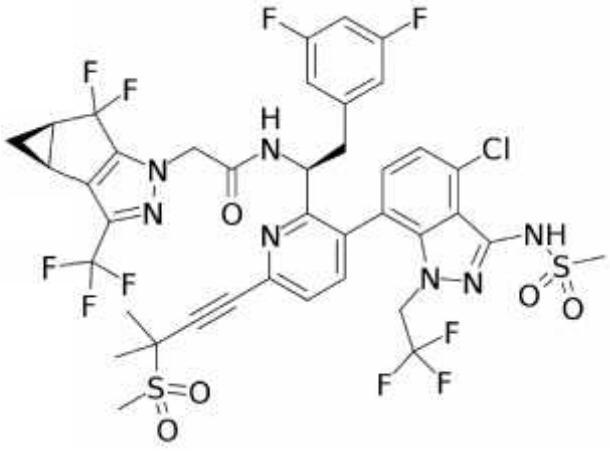
CAPSID INHIBITORS & LENACAPAVIR

14. Capsid is the name given to the proteins that surround HIV's genetic material. Upon HIV attaching itself to a target cell of the immune system, the virus sends its genetic material (RNA) into the cell. As the genetic material is surrounded by the capsid, it is protected from detection by the

[1] https://www.cdc.gov/hiv/basics/whatishiv.html
[2] http://naco.gov.in/hiv-facts-figures

cell's internal sensors. The capsid, along with its cargo of genetic material, then makes its way to the cell's control centre, or nucleus. Once near the nucleus, the capsid releases its cargo, and through a series of steps HIV's genetic material is converted into a form similar to the cell's genetic material (DNA). The capsid proteins then help HIV's DNA cross into the nucleus, where it integrates into the cell's DNA. At some point in the future, perhaps through immunological stimulation, the cell becomes activated and HIV's DNA takes over the cell and converts it into a mini-virus factory, producing new copies of HIV.

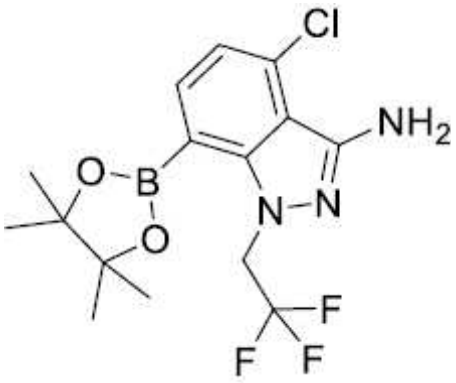
15. A capsid inhibitor could work by interrupting or impairing three different parts of HIV's life cycle. The HIV capsid has been extensively explored as a potential target to develop small molecules to target capsid protein which can interfere at both early and late steps in HIV replication cycle[3]. In theory, since the capsid inhibitor has so many anti-HIV activities, it could be used by itself in the prevention of HIV infection. Lenacapavir is a capsid inhibitor (formerly known as GS-6207) that disrupts the HIV capsid, the cone-shaped shell that surrounds the viral genetic material and essential enzymes. Laboratory studies showed that it interrupts multiple stages of the HIV life cycle. It has the following structure:



[3] "Inhibitors of HIV-1 Capsid, A target Opportunity"; Stephanie K Cranes, Jonathan H. Sheeshan etal, 13(4): 359-365, 2018 July. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6075716/

SUMMARY OF GROUNDS CONSIDERED FOR OPPOSITION

16. The Opponent submits that following claims are relevant to Lenacapavir and hence opposes the same:
    a. Claim 1 covering formula (Ia) and dependent claim 2
    b. Formulation claims 5 and 7-12 as they pertain to compound Ia
    c. Claim 6 covering the intermediate compound 12 required for preparation of compound Ia and Ib



17. Claim 3 and 4 are NOT relevant to Lenacapavir as compound IIa and IIb is structurally different from Iai.e.Lenacapvir with a cyclopropyl sulfonylamino substitution at Z^1 and hence not being opposed in present submission.

18. The Opponent bring this submission under the following grounds, each of which are without prejudice to one another and stand on an independent footing:

    i) S.25(1)(b)(i):

    'that the invention so far as claimed in any claim of the complete specification has been published before the priority date of the claim—

    (i) in any specification filed in pursuance of an application for a patent made in India on or after the 1st day of January, 1912'

    ii) S.25(1)(d):

'(d) that the invention so far as claimed in any claim of the complete specification was publicly known or publicly used in India before the priority date of that claim.

iii) S.25(1)(e):

'(e) that the invention so far as claimed in any claim of the complete specification is obvious and clearly does not involve any inventive step, having regard to the matter published as mentioned in clause (b) or having regard to what was used in India before the priority date of the applicant's claim;'

iv) S.25(1)(f):

'(f) that the subject of any claim of the complete specification is not an invention within the meaning of this Act, or is not patentable under this Act;'

v) S.25(1)(g):

'(g) that the complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed;'

DISCUSSION OF RELEVANT PRIOR ART:

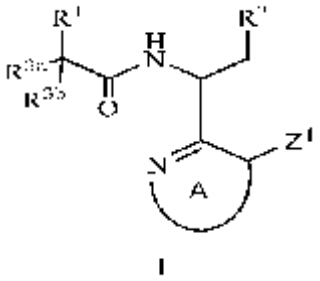
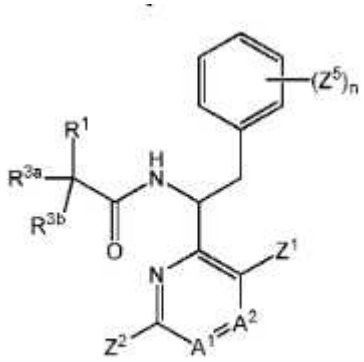
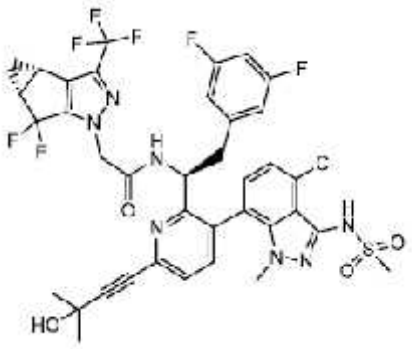
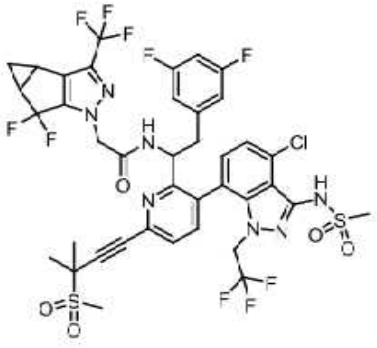
19. The Opponent will be using the following prior art documentsand numbering scheme throughout its submissions:

D1: WO2014134566, hereinafter referred to as D1 or '566.The IPO has cited its family member US20140303164in its Examination. D1 was filed in India as 7440/DELNP/2015.Opponent will use D1 or '7440 interchangeably, depending on the context.

D2: WO2013006738 [published on 10/Jan/2013].Family to US20140142085.

D3: WO2016033243 [published on 03/Mar/2016]. Family to US20160083368.

20. D1 i.e.WO2014134566, titled '*AMIDE COMPOUNDS FOR THE TREATMENT OF HIV*' is an important publication. This PCT comes from the present Applicant itself (Gilead). It bears an earliest priority of March 2013 and was published on 04/Sep/2014, thus it was published much before the priority of present '277 filing. D1 discloses compounds or salts thereof for treating Retroviridae viral infection including an infection caused by the HIV virus. It goes further and discloses pharmaceutical compositions for these compounds, processes for preparing these compounds, intermediates useful for preparing these compounds.Following compounds of D1 – i.e. compound IIId and compounds covered in amended claim 27 of corresponding Indian 7440 file are coveredwithin compounds having formula 1:

D1: Formula I	D1: formula IIId
 I	 IIId
D1: Claim 39	Present '277: Claim 1- compound 1a
	 (Ia)

21. While the specific substitutions will be dealt in the latter segments, the Opponent submits that Lenacapvir specific compound is completely covered within the Markush disclosure of D1. Simply put, when appropriate substitutionsthat are within the D1 disclosure, are made to compound IIId, we get the compounds of present claims i.e.Lenacapavirwith formula Ia and Ibwhich is squarely covered within the D1 disclosure.

22. **D2**i.e.WO2013006738, titled '*COMPOUNDS FOR THE TREATMENT OF HIV*' is another important publication from present Applicant. It bears an earliest priority of July 2011 and was published on 10/Jan/2013, thus it was published much before the priority of present '277 filing. D2 discloses compounds for treating or preventing infection caused by the HIV virus.

23. **D3**: WO2016033243 carries a published dateof 03/Mar/2016i.e. much before the priority of present '277 filing. D3 is also from present Applicant (Gilead) and titled '*ANTIRETROVIRAL AGENTS*'. D3 also has a similar markush coverage as present '277 seeks to cover and discloses the substitutions to the cental pyridine ring at the terminal position.

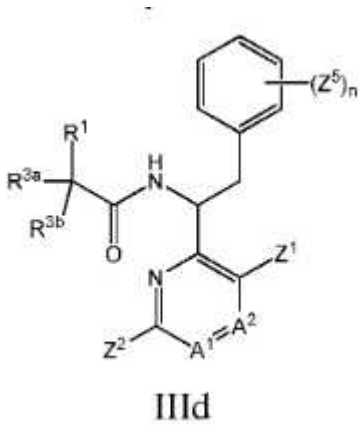
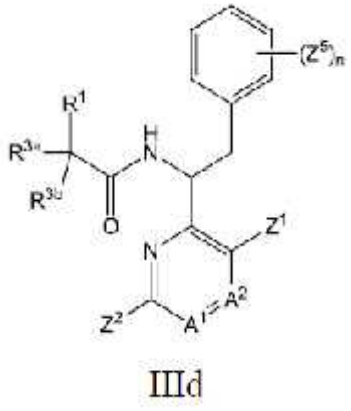
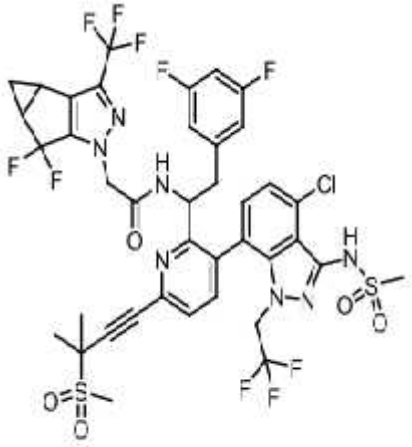
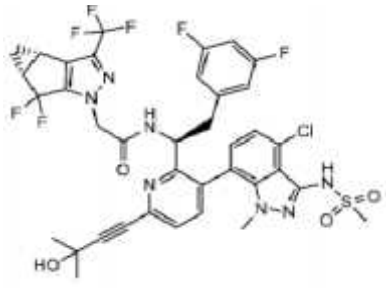
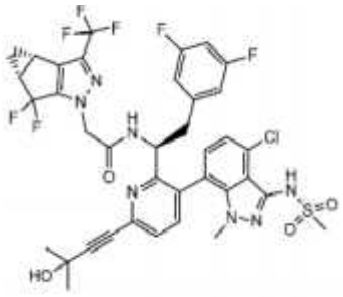
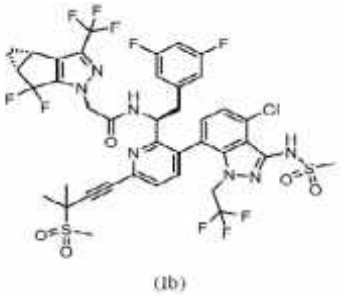
DETAILED GROUNDS

I. THAT CLAIMS OF THE PRESENT APPLICATION MUST BE REJECTED AS THE CLAIMED INVENTION WAS PUBLISHED BEFORE THE PRIORITY DATE OF PRESENT SPECIFICATION AND CLAIMS

24. As noted earlier, document **D1**i.e. WO2014134566was published on 04/Sep/2014. Its Indian national phase filing (7440/DELNP/2015) was published on 15/Jan/2016. Hence, both these documents were published much before the priority of present '277 filingi.e. 19/Aug/2016.

25. **D1** discloses compounds or salts thereof. It goes further and discloses/ teaches pharmaceutical compositions for such compounds, processes for preparing these compounds and intermediates useful for preparing these

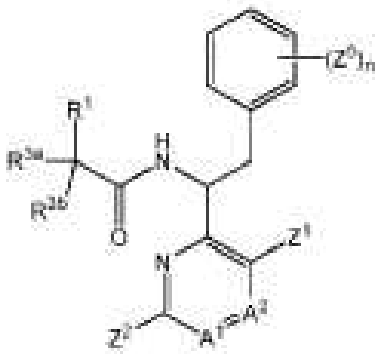
compounds. Following compounds of D1 – i.e. compound IIId and compounds covered in D1' claims38 and 39 are covered within compounds within formula 1. Further, the same applicant (Gilead) in the amended set of claims for 7440/DELNP/2015 application specifically covers the claimed compounds in both markush with formula IIId and compound Ia which is derived from the Markush Formula IIId. The below table provides a comparison between D1, equivalent Indian application with the amended claims of the impugned application:

D1 - **WO2014134566**	7440/DELNP/2015 – Amended claims (Total 36)	Impugned Application (It directly claims the compound)
Claim 1  IIId	Claim 1  IIId	Claim 1  (Ia)
Claim 39 	Claim 28 	Claim 2  (Ib)

26. The Opponent submits that compound Ia of present claims (i.e.Lenacapavir specific compound) is completely covered within the Markush disclosure of compound IIIdof D1. Simply put, when appropriate substitutions that are clearly within the D1 disclosureare made to compound IIId, we get the compounds of present claims i.e.Lenacapavir (including its pharmaceutically acceptable salts)and is squarely covered within the D1 disclosure. The claimed invention of present '277 was clearly published in D1 before the priority date of present Specification and claims. The below highlighted portion in WO claim 1 (compound IIId) is Lenacapavir. The same compound is specifically covered in the amended set of claims of 7440/DELNP/2015 application, in particular substitution at Z^1 covers 5-14 membered heteroaryl and substitution at Z^2 position covers (C_2-C_8) alkynyl, itnarrows it down to compound Ia (Lenacapavir) of the present'277 application.

D1: discussion on how it covers Lenacapavir:

1. A compound of formula IIId:



wherein

A 1 is CH, C-Z 3 , or nitrogen;

A is CH or nitrogen;

R^1 is 6-12 membered aryl, 5-12 membered heteroaryl, or 3-12 membered heterocycle, wherein any 6-12 membered aryl, 5-12 membered heteroaryl, or

3-12 membered heterocycle of R^1 is optionally substituted with 1, 2, 3, 4 or 5 Z^4 groups, wherein the Z^4 groups are the same or different;
each R^{3a} and R^{3b} is independently H or $(C_1$-$C_3)$alkyl;

Z^1 is 6-12 membered aryl, 5-14 membered heteroaryl, or 3-14 membered heterocycle, wherein any 6-12 membered aryl, 5-14 membered heteroaryl, or 3-14 membered heterocycle of Z is optionally substituted with 1, 2, 3, 4 or 5 Z^{la} or Z^{lb}, wherein the Z^{la} and Z^{lb} groups are the same or different;

each Z^{la} is independently $(C_3$-C7)carbocycle, 5-12 membered heteroaryl, 3-12 membered heterocycle, halogen, -CN, $-OR^{nl}$, $-OC(0)R^{pl}$, $-OC(0)NR^{ql}R^{rl}$, $-SR^{nl}$, $-S(0)R^{pl}$, $-S(0)_2OH$, $-S(0)_2R^{pl}$, $-S(0)_2NR^{ql}R^{rl}$, $-NR^{ql}R^{rl}$, $-NR^{nl}COR^{pl}$, $-NR^{nl}C0_2R^{pl}$, $-NR^{nl}CONR^{ql}R^{rl}$, $-NR^{nl}S(0)_2R^{pl}$, $-NR^{nl}S(0)_2OR^{pl}$, $-NR^{nl}S(0)_2NR^{ql}R^{rl}$, $-C(0)R^{nl}$, $-C(0)OR^{nl}$, $-C(0)NR^{ql}R^{rl}$ and $-S(0)_2NR^{nl}COR^{pl}$, wherein any $(C_3$-$C_7)$carbocycle, 5-12 membered heteroaryl and 3-12 membered heterocycle of Z^{la} is optionally substituted with 1, 2, 3, 4 or 5 Z^{lc} or Z^{ld} groups, wherein the Z^{lc} and Z^{ld} groups are the same or different;

each Z^{lb} is independently $(C_1$-$C_8)$alkyl optionally substituted with 1, 2, 3, 4 or 5 halogen, which are the same or different;

each Z^{lc} is independently halogen, -CN, -OH, $-NH_2$, $-C(0)NR^{q2}R^{r2}$, or $(C_1$-$C_8)$heteroalkyl;

each Z is independently $(C_1$-Cg)alkyl or $(C_1$-Cg)haloalkyl;

each R^{nl} is independently H, $(C_1$-$C_8)$alkyl, $(C_3$-$C_7)$carbocycle, 3-7 membered

heterocycle, or 5-6 membered monocyclic-heteroaryl, wherein any $(C_3$-$C_7)$carbocycle, 3-7 membered heterocycle, or 5-6 membered monocyclic-heteroaryl of R^{nl} is optionally substituted with 1, 2, 3, 4 or 5 Z^{lc} or Z^{ld} groups, wherein the Z^{lc} and Z^{ld} groups are the same or different, and wherein any (Ci-

C8)alkyl of R^{nl} is optionally substituted with 1, 2, 3, 4 or 5 Z^{lc} groups, wherein the Z^{lc} groups are the same or different;

each R^{pl} is independently (C_1-C_8)alkyl, (C_3-C_7)carbocycle, 3-7 membered heterocycle, or 5-6 membered monocyclic-heteroaryl, wherein any (C_3-C_7)carbocycle, 3-7 membered heterocycle, or 5-6 membered monocyclic-heteroaryl of R^{pl} is optionally substituted with 1, 2, 3, 4 or 5 Z^{lc} or Z^{ld} groups, wherein the Z^{lc} and Z^{ld} groups are the same or different, and wherein any (C_1-Cg)alkyl of R^{pl} is optionally substituted with 1, 2, 3, 4 or 5 Z^{lc} groups, wherein the Z^{lc} groups are the same or different;

each R^{ql} and R^{rl} is independently H, (C_1-Cg)alkyl, (CrC$_7$)carbocycle, 3-7 membered heterocycle, or 5-6 membered monocyclic-heteroaryl, wherein any (C3-C_7)carbocycle, 3-7 membered heterocycle, or 5-6 membered monocyclic-heteroaryl of R^{ql} or R^{rl} is optionally substituted with 1, 2, 3, 4 or 5 Z^{lc} or Z^{ld} groups, wherein the Z^{lc} and Z^{ld} groups are the same or different, and wherein any (C_1-Cg)alkyl of R^{ql} or R^{rl} is optionally substituted with 1, 2, 3, 4 or 5 Z^{lc} groups, wherein the Z^{lc} groups are the same or different, or R^{ql} and R^{rl} together with the nitrogen to which they are attached form a 5, 6 or 7-membered heterocycle, wherein the 5, 6 or 7-membered heterocycle is optionally substituted with 1, 2, 3, 4 or 5 Z^{lc} or Z^{ld} groups, wherein the Z^{lc} and Z^{ld} groups are the same or different;

each R^{q2} and R^{r2} is independently H, (Ci-Cg)alkyl, (C_3-C_7)carbocycle, or R^{q2} and R^{r2} together with the nitrogen to which they are attached form a 5, 6, or 7-membered heterocycle;

Z^2 is (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, 6-12 membered aryl, 5-12 membered C-linked-heteroaryl, 3-12 membered C-linked-heterocycle, -C(0)R^{n3}, or -C(0)N$R^{q3}R^{r3}$, wherein any 6-12 membered aryl, 5-12 membered C-linked-heteroaryl, or 3-12 membered C-linked-heterocycle of Z^2 is optionally

substituted with 1, 2, 3, 4 or 5 Z^{2b} or Z^{2c} groups, wherein the Z^{2b} and Z^{2c} groups are the same or different, and wherein any (C_2-Cg)alkenyl or (C_2-Cg)alkynyl of Z is optionally substituted with 1, 2, 3, 4, or 5 Z^{2c} groups, wherein the Z^{2c} groups are the same or different; each R^{n3} is independently H or (Ci-C_4)alkyl;

each R^{q3} and R^{r3} is independently H or (Ci-C_4)alkyl;

each Z is independently oxo, (C_1-C_4)alkyl, (C_1-C_4)heteroalkyl or (C_1-C_4)haloalkyl; each Z^{2c} is independently oxo, halogen, -CN, -OR^{n4}, -$OC(0)R^{p4}$, -$OC(0)NR^{q4}R^{r4}$, -SR^{n4}, -$S(0)R^{p4}$, -$S(0)_2OH$, -$S(O)_2R^{P4}$, -$S(0)_2NR^qV^4$, -NR^qV^4, -$NR^{n4}COR^{p4}$, -$NR^{n4}C0_2R^{p4}$, -$NR^{n4}CONR^{q4}R^{r4}$, -$NR^{n4}S(0)_2R^{p4}$, -$NR^{n4}S(0)_2OR^{p4}$, -$NR^{n4}S(0)_2NR^{q4}R^{r4}$ -$N0_2$, -$C(0)R^{n4}$, -$C(0)OR^{n4}$, or -$C(0)NR^qV^4$;

each R^{n4} is independently H, (Ci-C_4)alkyl, (C_1-C_4)haloalkyl, or (C_1-C_4)heteroalkyl;
each R^{p4} is independently (C_1-C_8)alkyl, (C_1-C_4)haloalkyl, or (C_1-C_4)heteroalkyl;

each R^{q4} and R^{r4} is independently H, (C_1-C_4)alkyl, (C_1-C_4)haloalkyl, or (Q-C_4)heteroalkyl;

each Z is independently a (C_1-C_4)heteroalkyl;

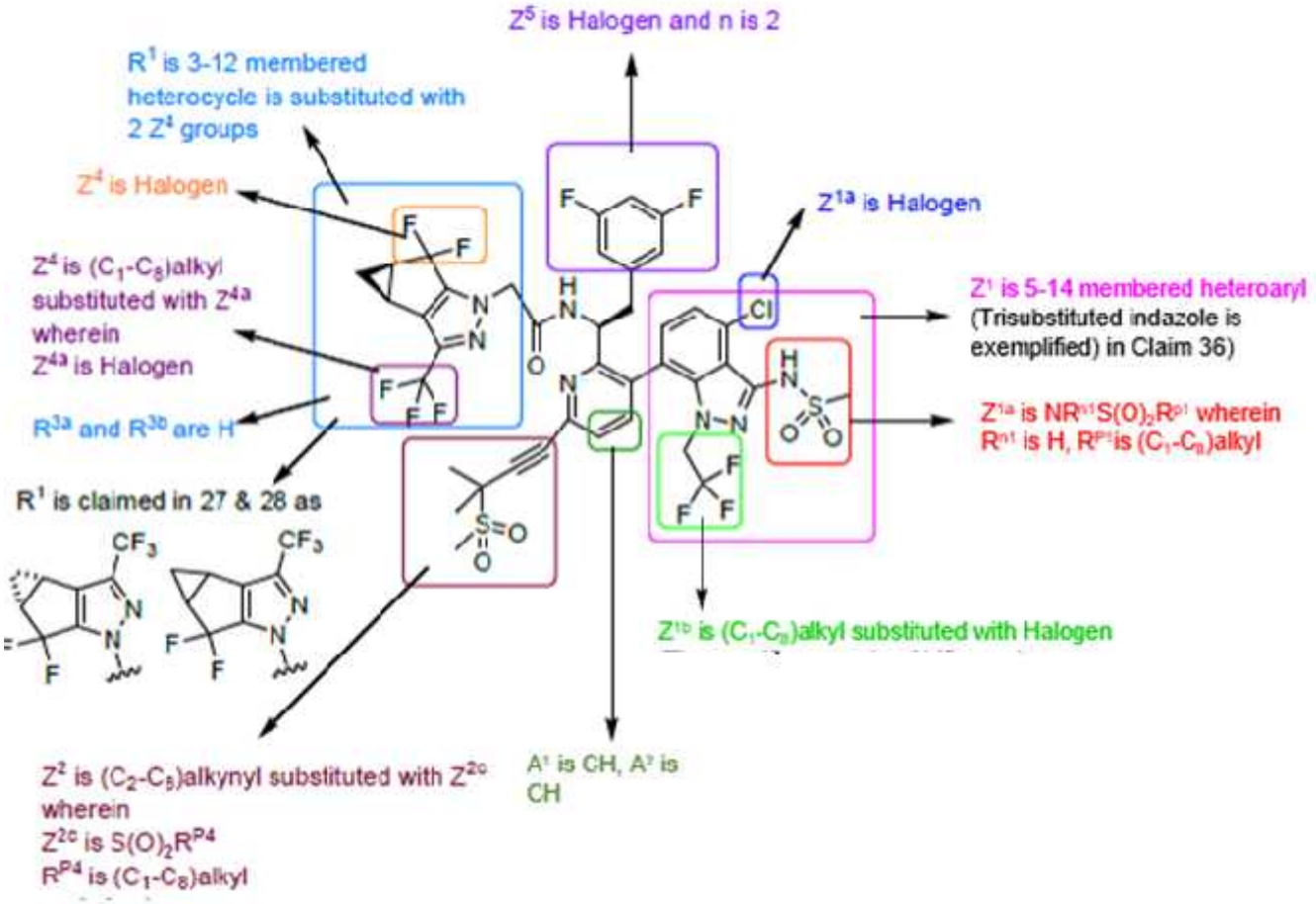
each Z^4 is independently oxo, (Ci-C_8)alkyl, (C3-C_7)carbocycle, halogen, -CN, -OR^{n5}, -$NR^{q5}R^{r5}$, -$NR^{n5}COR^{p5}$, -$NR^{n5}C0_2R^{p5}$, -$C(0)R^{n5}$, -$C(0)OR^{n5}$, or -$C(0)NR^{q5}R^{r5}$, wherein any (C_3-C_7)carbocycle or (C_1-C8)alkyl of Z^4 is optionally substituted with 1, 2, 3, 4 or 5 Z^{4a} groups, wherein the Z^{4a} groups are the same or different;

each Z^{4a} is independently halogen, -CN, or -OR^{n6};

each R^{n5}, R^{p5}, R^{q5}, R^{r5}, and R^{n6} is independently H or (Ci-C_4)alkyl;

each Z^5 is independently halogen, which may be same or different; and n is 0, 1, 2, or 3; or a pharmaceutically acceptable salt thereof.

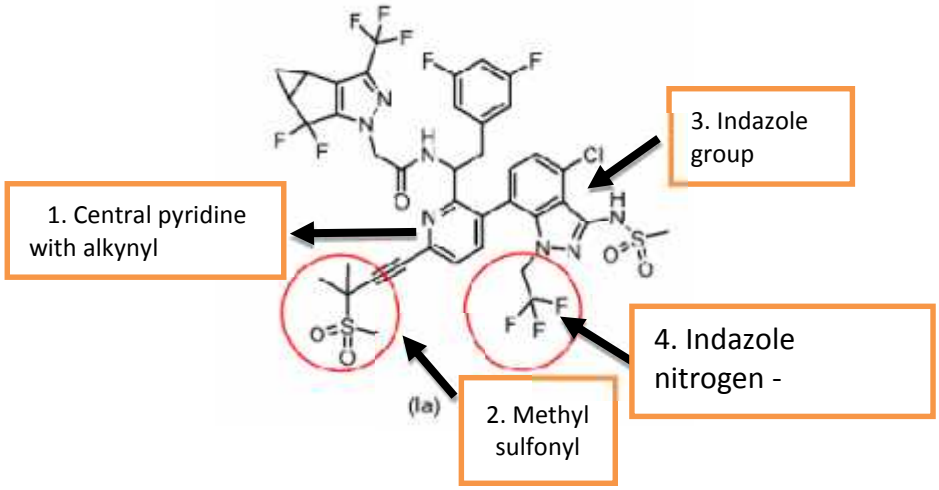
27. Specifically, when we put appropriate substitutions disclosed in D1 on a compound of formula IIIdinclaim 1 along with the components given in claims 37 and 39, we get the following compound:



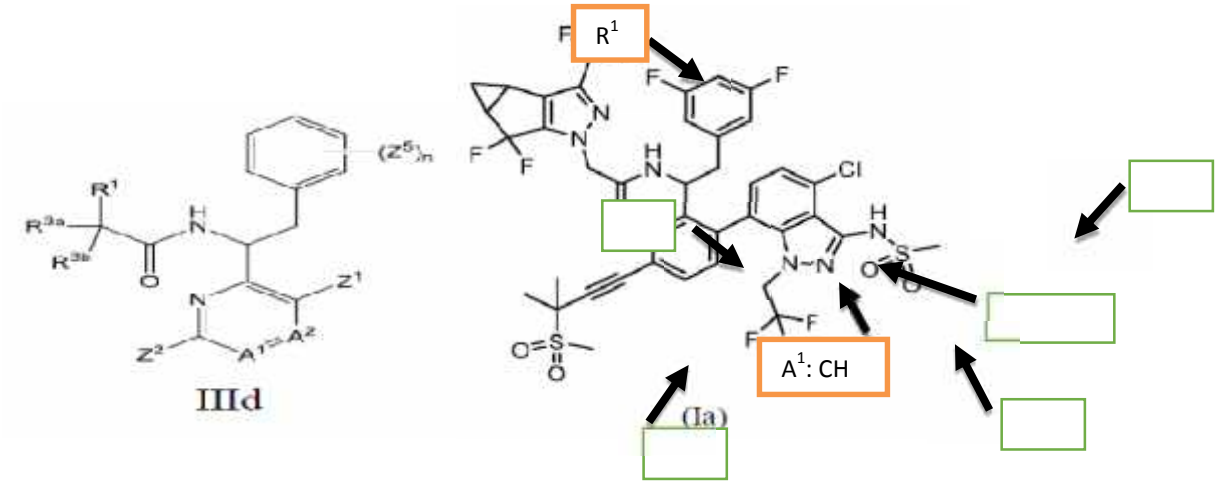
29. The above discussion of D1 and its compound IIId with the presently claimed compound Ia of '277 is again represented belowin a format as submitted by the Applicant in its post hearing submissions for present '277 application.The Applicant's assertion that there is no disclosure in D1 to

arrive at claimed compound Formula Ia with the below listed substitutions at Z^1 and Z^2 is inaccurate.

30. Opponent submits that following substitutions at Z^1 and $Z^2$is already covered in Markush formula IIId:
    1. Substitution of the central pyridine with a substituted alkynyl
    2. Substitution of alkynyl with a methyl sulfonyl group
    3. Substitution of the central pyridine with a substituted indazole group
    4. Substitution of indazole nitrogen with a trifluroethyl (Ia) and difluroethyl (IIa)



31. IIId of D1 covers the claimed compound with formula Ia of claim 1 of present '277 Application. All the key substitutions is covered and claimed in both D1 document and its equivalent Indian application 7440/DELNP/2015.



32. To further explain the coverage of the claimed compound Lenacapavir in D1 with formula Ia of the impugned application, the chemical name of Lenacapavir [compound 24] is listed against the markush formula. Chemical name: 1H-Cyclopropa[3,4]cyclopenta[1,2]pyrazole-1-acetamide, N-[(1S)-1-[3-[4-chloro-3- [(methylsulfonyl)amino]-1-(2,2,2-trifluoroethyl)-1H-indazol-7-yl]-6-[3-methyl-3-(methylsulfonyl)-1-butyn-1-yl]-2-pyridinyl]-2-(3,5-difluorophenyl)ethyl]-5,5-difluoro-3b,4,4a,5-tetrahydro-3-(trifluromethyl)-,(3bS, 4aR)

{Chemical name listed against each markush substitution}

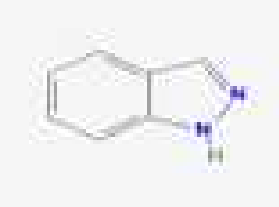
A^1 is CH; A^2 is CH][-2-pyridinyl]

R^1 is 3-12 member heterocycle [1H-Cyclopropa[3,4]cyclopenta[1,2]pyrazole-1-acetamide]

R^1 is optionally substituted with 1, 2, 3, 4 or 5 Z^4 groups, wherein the Z^4 groups are same or different [1H-Cyclopropa[3,4]cyclopenta[1,2]pyrazole-1-acetamide]

Each R^{3a} and R^{3b} is independently H [1H-Cyclopropa[3,4]cyclopenta[1,2]pyrazole-1-acetamide]

Z^1 is 3-14 membered heterocycle **[includes Indazole a heterocyclic aromatic compound]** [N-[(1S)-1-[3-[4-chloro-3-[(methylsulfonyl)amino]-1-(2,2,2-trifluoroethyl)-1H-indazol-7-yl]



Z^1 3-14 membered heterocycle is optionally substituted with 1, 2, 3, 4 or 5 Z^{1a} and Z^{1b} groups, wherein Z^{1a} and Z^{1b} groups are same or different [N-[(1S)-1-[3-[4-chloro-3-[(methylsulfonyl)amino]-1-(2,2,2-trifluoroethyl)-1H-indazol-7-yl]

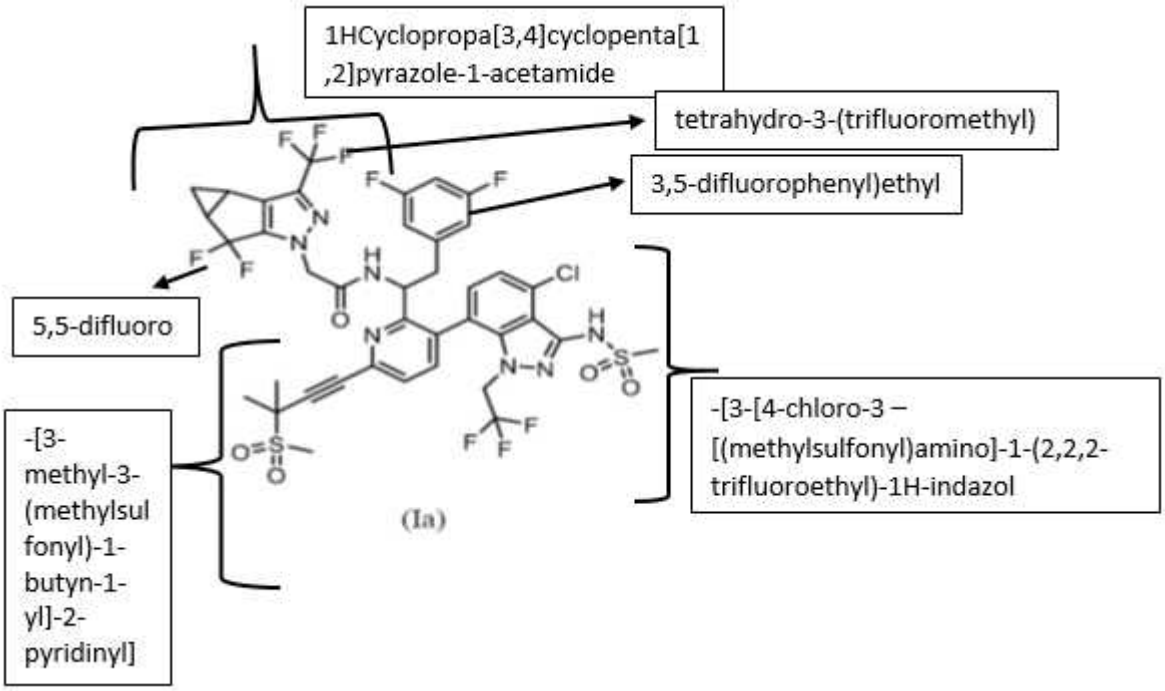
Each Z^{1a} is halogen; $NR^{n1}S(O)_2R^{p1}$, each NR^{n1} is independently H, each R^{p1} is 5-6 membered monocyclic heteroaryl [N-[(1S)-1-[3-[4-chloro-3-[(methylsulfonyl)amino]-1-(2,2,2-trifluoroethyl)-1H-indazol-7-yl]

Each Z^{1b} is independently (C_1-C_8) alkyl optionally substituted with 1, 2, 3, 4 or 5 halogen[N-[(1S)-1-[3-[4-chloro-3-[(methylsulfonyl)amino]-1-(2,2,2-trifluoroethyl)-1H-indazol-7-yl]

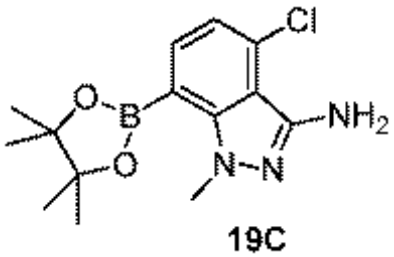
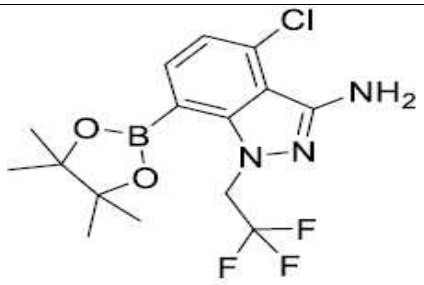
Z^2 is (C_2-C_8) alkynyl optionally substituted with 1, 2, 3, 4 or 5 Z^{2c} groups, wherein Z^{2c} groups are same or different [3-methyl-3-(methylsulfonyl)-1-butyn-1-yl]-2-pyridinyl]

Z^{2c} is independently $–S(O)_2R^{p4}$, each R^{p4} is independently (C_1-C_8) alkyl [3-methyl-3- (methylsulfonyl)-1-butyn-1-yl]-2-pyridinyl]

33. 1H-Cyclopropa[3,4]cyclopenta[1,2]pyrazole-1-acetamide, N-[(1S)-1-[3-[4-chloro-3- [(methylsulfonyl)amino]-1-(2,2,2-trifluoroethyl)-1H-indazol-7-yl]-6-[3-methyl-3-(methylsulfonyl)-1-butyn-1-yl]-2-pyridinyl]-2-(3,5-difluorophenyl)ethyl]-5,5-difluoro-3b,4,4a,5-tetrahydro-3-(trifluoromethyl)-, (3bS,4aR



34. Claim 6 of present application stands generically covered. Please see claim number 5,6,7,8, 29, 30, 31, 33, 34, 35 and 36 of the D1 i.e. WO'566 for reference. All the substituents are listed.The synthesis for the preparation of the compound 12 as claimed in claim 6 is also disclosed in D1. The intermediate compound 19C disclosed in WO'566 (refer Example 19, at page no.150, Example 58, at page no.190 and Example 171 at page no.309 is similar to the intermediate compound of the impugned application). Similar intermediate is used to arrive at the claimed compound Ia and Ib in the impugned application.

D1 – WO2014/134566	Impugned Application Claim 6
 19C	

35. D1 also specifically enables and covers various "Pharmaceutically acceptable salt" of IIId and states the following:

'[56] Examples of "pharmaceutically acceptable salts" of the compounds disclosed herein include salts derived from an appropriate base, such as an alkali metal (for example, sodium),

... Representative non-limiting lists of pharmaceutically acceptable salts can be found in S.M. Berge et al., J. Pharma Sci., 66(1), 1-19 (1977), and Remington: The Science and Practice of Pharmacy, R. Hendrickson, ed., 21st edition, Lippincott, Williams & Wilkins, Philadelphia, PA, (2005), at p. 732, Table 38-5, both of which are hereby incorporated by reference herein.

... All salts, whether or not derived from a physiologically acceptable acid or base, are within the scope of the present invention.

[0058] Metal salts typically are prepared by reacting the metal hydroxide with a compound disclosed herein. Examples of metal salts which are prepared in this way are salts containing Li+, Na+, and K+. A less soluble metal salt can be precipitated from the solution of a more soluble salt by addition of the suitable metal compound.'

36. D1 also covers formulations (including parenteral formulations) of compound IIId and salts of compound IIId. Specifically, para 381 and example 202 at para 875 cover injectable formulations of compounds of D1, thereby including IIId.Thus, D1 clearly covers sodium salt of compound IIId and also advises the Person Skilled in the Art to refer to the standard books on what salts can be made and how they can be made as well parenteral formulations of such compounds.

37. Importantly, the Opponent submits that the Applicant via D1s' Indian filing 7440/DELNP/2015, is already seeking a *Markush* patent encompassing Lenacapavir. This D1/ 7440 application, if granted an Indian patent, shall expire on 28/Feb/2034 – blocking 3rd parties from making Lenacapavir, its salts and formulations of Lenacapavir. Thus, the present application ('277)

that carries an international filing date of 17/Aug/2017, is nothing but an ill-founded attempt at extending the monopoly on Lenacapavir compound and formulations thereof from Feb 2034 through to Aug 2037.

38. The Hon'ble Supreme Court of India too in *Novartis AG v. Union of India*, [(2013) 6 SCC 1] has also discussed the issue of evergreening of patents. The Patents Act should be interpreted by the Hon'ble Patent Controller in light of all the relevant circumstances surrounding the Amending Act. The Hon'ble Madras High Court, in*Novartis AG v. Union of India and Others, (2007) 4 MLJ 1153*, while upholding Section 3(d) against a constitutional challenge, stated: "We have borne in mind the object which the Amending Act wanted to achieve namely, ***to prevent evergreening; to provide easy access to the citizens of this country to life saving drugs and to discharge their Constitutional obligation of providing good health care to its citizens.***" [see para 19] (emphasis added).

39. Accordingly, as D1 clearly covers claims 1, 2,6, 5, 7-12 of present '277 and hence these claims are liable to be rejected in totality.

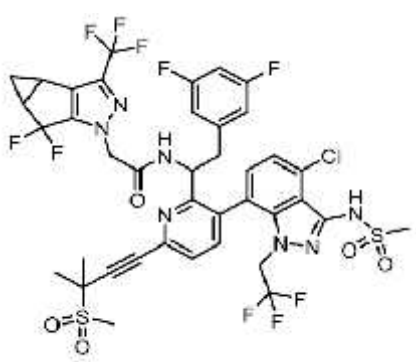
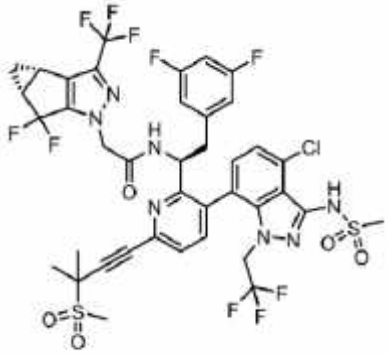
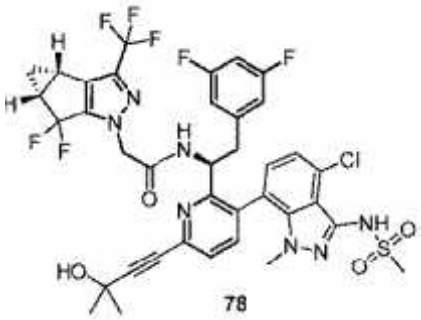
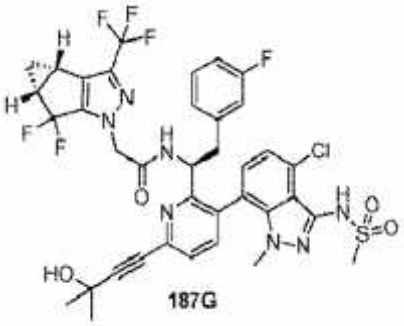
II. CLAIMS OF THE PRESENT APPLICATION ARE CHALLENGED UNDER SECTION 25(1)(e) OF THE PATENTS ACT, ON GROUND OF LACKING INVENTIVE STEP AS DEFINED UNDER SECTIONS 2(1)(ja) OF THE PATENTS ACT

40. Section 2(1)(j), requires that an invention be either a new product or process involving an inventive step and capable of industrial application. 'Inventive step' is further defined in Section 2(1)(ja) as 'a feature of an invention that involves technical step as compared to existing knowledge ..'.

41. Independent of the Opponent'santicipation argument from D1, the Opponent now submits, that D1, in combination with other documents renders the present claims as non-patentable as the claims are found

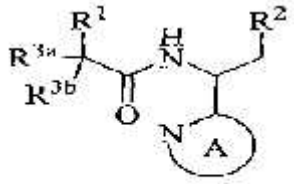
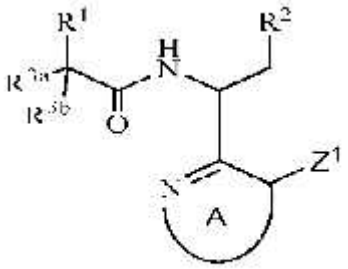
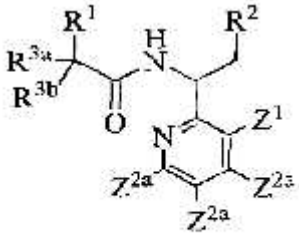
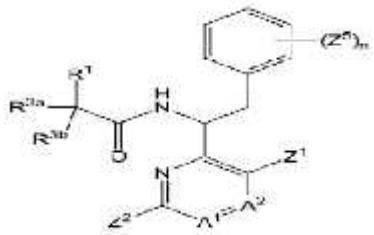
obvious and lacking an inventive step. Specifically, D1, when combined with D2 render the claims as obvious/ lacking inventive step.

42. Again starting from D1, the following compounds are clearly disclosed therein which is similar to the claimed compound Ia / Ib. In particular reference is made to the below listed compounds 78 and 187G (one Flourine is missing)of D1 with structures similar to the claimed compound Ia/Iband thereby render the claimed compounds obvious.

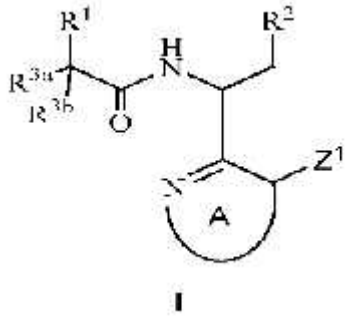
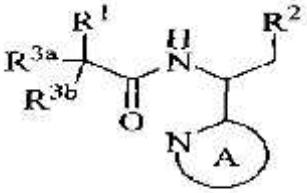
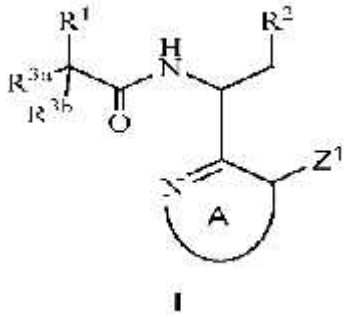
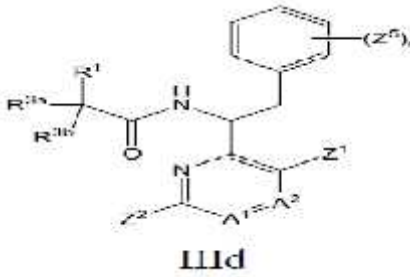
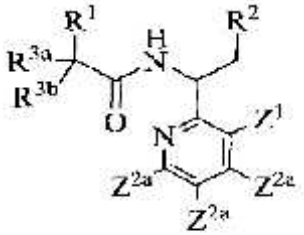
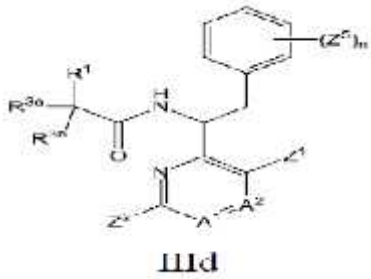
<table>
<tr><td colspan="2">Claimed Compound Ia / Ib of present '277
 
(Ia)
 
(Ib)</td></tr>
<tr><td colspan="2">Compounds from D1:</td></tr>
<tr><td> 
78</td><td> 
187G</td></tr>
</table>

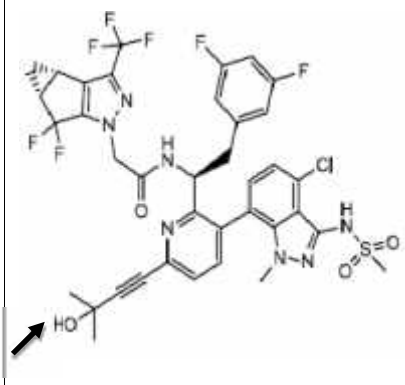
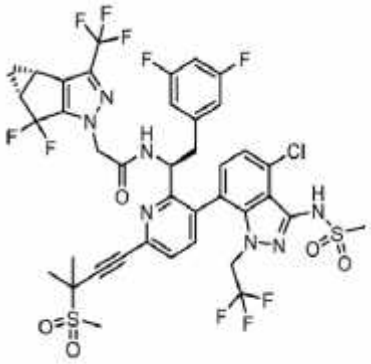
43. D2 also discloses compounds similar to those claimed in present Application. D2 discloses compounds for treating or preventing infection caused by the HIV virus. The markush formulaIIId from which the claimed compound is derived is disclosed in D2 and they all belong to the same chemical genus derived from the same markush structure. The below table

provides the comparison of the markush disclosed in D2 and the same mentioned in the present application by the applicant.

D2: WO2013006738	Present '277 Application
 **Line no.10, page no.15, Ibb**	 I **Formula I**
 Idd	 IIId

44. When we combine the teachings of D1 and D2 and view them in comparison to present Application, it is evident from the below table, that the compounds claimed are obvious from the prior art disclosures starting with the markushformula, IIIdmarkush compound and the listed substituents as mentioned in the preceding paragraphs.In particular claim 39 of D1 is similar to claimed compounds Ia /Ib with minor variation in the structure. Given the know-how for the possible substituents to the markush structure and the list of substituents disclosed in the D1 and D2 prior art documents, the claimed compound is found to be obvious.

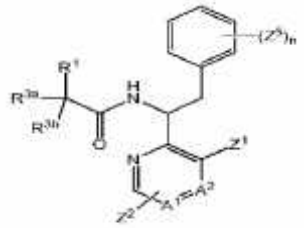
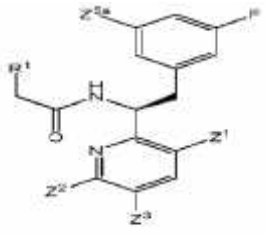
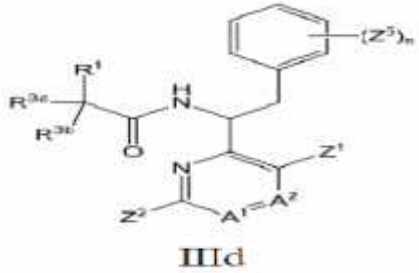
D1: WO2014134566	D2: WO2013006738	Present Application IN'277
 I **Formula III**	 **Line no.10, page no.15, Ibb**	 I **Formula I**
 IIId	 Idd	 IIId At page no.6 of specificationabove structure IIIdis included and mentioned asapart from this disclosure compounds that are potent and stable and exhibit improved pharmacokinetic or pharmacodynamic

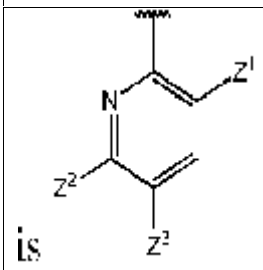
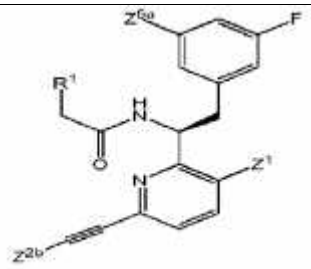
		profiles for treatment of a Retroviridae viral infection are required. So the present claimed compounds with formula Ia, Ib, IIa and IIb all belong to the same genus derived from same markush structure.
 Claim 39 is same as Lenacapavir except for pointed out difference. However the markush compound IIId includes the listed substituents		 (Ib) Compound 24 mentioned as Ia in submissions, however in the specification Ib is mentioned as compound 24.

45. Gilead's **D3** covers the same markush structure and use of the listed compound in the treatment of HIV. Very importantly, D3 discloses the substitution to the central pyridine ring at the terminal position, therefore the claim made by the applicant in their submission to the Controller that skilled person cannot arrive at the claimed compound in absence of knowing the structure of the claimed compound is incorrect.

Suggestion / Motivation for Z1 and Z2 substitutions on core moiety:

46. A combined reading of D1, D2 and D3 state of art informs a POSITA the markush structure, a list of possible substitutions to these markush structure, the antiviral activity of the listed compounds and the possibility of substitutions at position Z^1 and Z^2 to arrive at the claimed compounds. The Opponent submits that Gilead's D3 when combined with D1, a person having ordinary skill in the art can look at a list of possible substitutions to these markush structure of D1 and the substitutions mentioned therein, the antiviral activity of the listed compounds as well as the compounds enunciated in D3 and the possibility of substitutions at position Z^1 and Z^2 to arrive at the claimed compound and thus claimed compound is rendered obvious.D3 also claims the markush compound IIId as formula I from which the claimed compounds of the impugned application is derived.

D3:WO2016033243	**Present '277 Application**
 I Claim 1  II	 IIId Refer the specification at page no.6.

Claim 10	
 is Claim 7, one of the moiety listed is as above with substitutions at Z^1 and Z^2 disclosed.	
 III In particular D3 discloses the subsitution of central pyridine ring i.e. at Z^2 of the present application. Refer claims 17 to 21.	

47. From the above discussion of the prior art documents D1, D2 and D3 the following elements of the claimed compounds stand disclosed. Thechemical genus of amide compounds, its synthesis and preparation, its use as therapeutic compound for treating Retroviridae viral infection including HIV infection, themarkushcompounds including markush compoundwith formulaIIIdand thelist of possible substituents of markush compound with formula IIIdwhich possess antiviral activity.In particular, D1 with markush compound formula IIId lists all the relevant substitutions of the claimed compound Ia/Ib.

48. Therefore, submissions made by the applicant that substitutions at position Z^1 and Z^2 in the claimed compound is inventive over the prior art disclosure is erroneous and is not supported by any data. A POSITA is motivated and guided by the available disclosures and will accordingly arrive at the claimed compound. The Ia/Ib compound of present '277 application is only a minor variation from compound of claim 39 of D1 and the listed substituents at position Z^1 and Z^2 of markush compound formulaIIId makes the claimed compounds obvious.

49. It is further emphasized that most of the above prior art documents are from Gilead, thereby establishing the fact that Applicant already is aware of the know-how around present compounds including present '277 claims. The markush structure of the lead compound remains the same since the disclosure was made much before the year 2018 starting from D1, in several patent documents from the Applicant itself. The Applicant has been making minor tweaks to a structure and filing multiple patents. The substitutions made to the markush structure in these prior art documents cover all the possible embodiments and multiple compounds can be obtained for the appropriate therapeutic effect. The Applicant continues to file multiple patent applications for same class of drugs with various substitutions to obtain multiple patent monopolies over iterations of the core markush.

50. The present '277 application also claims same set of compounds which is both structurally and functionally disclosed in D1 and for use in the treatment of HIV as disclosed in the prior art documents, therefore claims are found to be obvious and lacks inventive step. Thus, based on the disclosure of the D1, D2 and D3, a person skilled in the art can very well reach the compounds Ia/Ib with reasonable expectation that such compounds would work for treating HIV. A POSITA who is equipped with the state of art disclosed in D1, D2 and D3 would look at the multiple Gilead filings and would be motivated to adopt and experiment on the same lines to

arrive at various compounds for treating HIV and compositions containing them.

51. The IPO has to examine the inventive step for compounds Ia/Ib and formulations containing the same after examining the documents D1 toD3, the state of art as of filing of present '277. In a similar case, the Opponent submits that the Controller, while determining inventive step, has held that mere "replacement of alkyl and/or other group" to a known structure cannot be considered as technical advancement under S. 2(1) (ja) (See order dated 21.02.2020 of the Assistant Controller of Patents and Designs in the matter of patent application478/MUMNP/2015).

52. The Opponent submits that other jurisdictions have invalidated patents for specific compounds when a prior Markush patent covered the same, for instance, please refer South Korea decisions for Apixaban and Dapagliflozin.

53. Coming to the formulation claims, the Applicant seeks to cover long-acting injectable formulations of the claimed compounds. D1 and D2 both cover parenteral compositions covering its compounds (i.e.IIId etc.). Specifically, at page 347 of the published WO (D1), we also see clear examples for injections – which are the same as those in D2 (refer example 602):

"

(iv) Injection 1 (1 mg/ml)	mg/ml
Compound X= (free acid form)	1.0
Dibasic sodium phosphate	12.0
Monobasic sodium phosphate	0.7
Sodium chloride	4.5
1.0 N Sodium hydroxide solution (pH adjustment to 7.0-7.5)	q.s.
Water for injection	q.s. ad 1 mL

(v) Injection 2 (10 mg/ml)	mg/ml
Compound X= (free acid form)	10.0
Monobasic sodium phosphate	0.3
Dibasic sodium phosphate	1.1
Polyethylene glycol 400	200.0
1.0 N Sodium hydroxide solution (pH adjustment to 7.0-7.5)	q.s.
Water for injection	q.s. ad 1 mL

„

54. Long acting/ controlled release formulations have been known in the art for long- for instance for cancer or other disease categories. Even within category of HIV drugs, there is a plethora of prior art that specifically discusses long acting injectable formulations of HIV drugs.For instance, there is a whole host of literature that discusses long acting injectable formulations of HIV drugs like Nevirapine, Efavirenz, Rilpivirine and Cabotageravir.

55. Following is a general and non-limiting list of prior art documents that discusses long acting injectable formulations of HIV drugs, with their publication dates:

Author	**Title**	**Journal& Citation**	**Publication date**	**Relevance**
Gerbenvan'tKloster, Eva Hoeben et. Al. (D4)	**'Pharmacokinetics and Disposition of Rilpivirine (TMC278) Nanosuspension as a Long-Acting Injectable Antiretroviral Formulation'**	**ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, doi: 10.1128/AAC.015**	May 2010, p. 2042–2050	Article discusses Rilpivirine long acting injectable formulation having a surfactant + water for injection

		29-09		Specifically, Poloxamer 338 (Pluronics F108) is used as a surfactantto enhance solubility and stabilize the colloidal suspension against aggregation. [document attached]
Katia P. Seremeta, Diego A. Chiappetta, Alejandro Sosnik, (D5)	Poly(ε-caprolactone), Eudragit® RS 100 and poly (ε-caprolactone)/Eudragit® RS 100 blend submicron particles for the sustained release of the antiretroviral efavirenz	Colloids and Surfaces B: Biointerfaces Volume 102, Pages 441-449,	1/Feb/2013	Sustained release injectable formulation of efavirenz with Poly (β-caprolactone).
AuthoSpreen	'Long-acting	CurrOpin	Nov/2013	General review

WR, Margolis DA, Pottage JC Jr. (D6)	injectable antiretrovirals for HIV treatment and prevention'	HIV AIDS. 8(6):565-71		article that looks at long acting injectable formulations for Cabotegravir and Rilpivirine.
Neha Jindal, S.K. Mehta (D7)	'Nevirapine loaded Poloxamer 407/Pluronic P123 mixed micelles: Optimization of formulation and in vitro evaluation'	Colloids and Surfaces B: Biointerfaces Vol 129 (2015) pages 100–106	18/Mar/15	Optimsation of a Poloxamer 407/Pluronic P123 based injectable formulation of Nevirapine is discussed [document attached]
Landovitz RJ, Kofron R, McCauley M. doi:10.1097/COH.0000000000000219. (D8)	The Promise and Pitfalls of Long Acting Injectable Agents for HIV Prevention	CurrOpin HIV AIDS 2016;11(1):122-128.	Jan 2016	Review article that looks at long acting injectable formulations for Cabotegravir and Rilpivirine.
Glaxo	'Long acting	WO20160	31/Mar/1	Long acting

Smithkline (D9)	pharmaceutical compositions'	46786	6	injectable formulation for HIV drugs – specific mention of various polymers/ excipients a) Poloxamer 338 (claim 13); b) Polyethylene glycol (para 51 of Desc) c) Water (as carrier, para 111 of Desc) [document attached]

56. Present Applicant has not given any technical disclosure that can be construed as having an inventive step over above prior state of art. The '277 Applicant has merely combined generally known excipients for long acting drugs and then presented them in the Specification.

57. The Opponent has clearly shown how the compound claims as well as the formulation claims are not inventive over prior art and lack an inventive step. Accordingly, the present Opponent submits that the entire set of present claims (compound and formulation) are obvious for a POSITA and lacking an inventive step thereby failing to fulfill the requirement under Section 2(1)(j) and 2(1)(ja) of the Patents Act, 1970, based on documents

cited above, thus claims 1, 2, 6, 5, 7-12 of present '277 Application are liable to be rejected in totality.

III. CLAIMS OF THE PRESENT APPLICATION ARE CHALLENGED UNDER SECTION 25(1)(F) OF THE PATENTS ACT, ON GROUND OF NOT BEING PATENTABLE ON ACCOUNT OF SECTION S(d), 3(f) AND SECTION 3(e) AND THEREFORE ARE OBJECTED TO UNDER SECTION 25(1) (f)

58. Section 25(1)(f) of the Patents Act allows opposition to grant of patent on the ground of the claimed invention not being an invention within the meaning of the Patents Act, 1970. Section 25(1)(f) reads as follows:

"(1) Where an application for a patent has been published but a patent has not been granted, any person may, in writing, represent by way of opposition to the Controller against the grant of patent on the ground
.. (f) that the subject of any claim of the complete specification is not an invention within the meaning of this Act, or is not patentable under this Act."

59. Opponent submits that S.25(1)(f) applies to the present claims under multiple frames of analysis:
    a) That present 277 Specification fails on disclosing 'technical advance as compared to existing knowledge'- which is a requirement of Section 2(1)(ja)- that forms foundation for a rejection under Section 25(1)(e); and
    b) S.3(d) applies since presently claimed compounds (Ia/ Ib) are structurally very similar to compound 78 from D1 and enhanced efficacy data for compounds is Ia/ Ibnot given against such relevant compounds.
    c) S.3(e) applies to formulation claims5 and 7-12 – as they seek to cover a mere admixture with excipients.
60. Prior art D1 already encompasses present compounds Ia/ Ib. Compound 78from D1 are structurally closest to presently claimed compounds in claims 1 and 6. An inventive step requires a 'technical advance as compared

to existing knowledge'. It is this 'technical advance' which is the inventor's hardwork and for which he gets the monopoly. As of the filing date of present '277 Specification, as much as it pertains to compounds Ia/ Ib and formulations containing them, the Applicant had not made any 'technical advance' in the present '277 Specification over disclosure in D1 and other cited prior art and so there was no case of having an 'inventive step' presentin Specification.

61. Since no 'technical advance' actually came in via the '277 Specification (as Lenacapavir and long acting injectable formulations were disclosed much earlier), there is no 'inventive step' disclosed in the present Specification. Since the present Specification does not contain 'inventive step', thus to the extent that claims (1 through 12) seeking to cover Lenacapaviror aninjectable composition covering it as the invention, the Specification lacks an 'inventive step' and hence these claims cannot be granted in present form.

62. Opponent submits that S.3(d) applies since presently claimed compounds (Ia/ Ib) are structurally very similar to compound 78 from D1 and enhanced efficacy data for compounds is Ia/ Ib is not given against such relevant compounds. The data submitted in Applicant's response to Controller is irrelevant as it is comparing Ia/ Ib with other compounds A and B that are not mentioned (or are not relevant) in the D1 document. Comparing Ia/Ib to compounds A and B is an incorrect comparison and one that is not looking at the afore-mentioned compound.

63. Unless, Applicant can show enhanced efficacy against the right set of structurally similar compounds (in this case, compound 78 from D1) or explain how / what are compounds A and B from D1 and how they are the 'appropriate' known substance for S. 3(d) examination, it cannot pass the burden of Section 3(d) and the compound claims will be liable to be rejected u/s 3(d).

64. The Opponent submits that the Applicant via D1s' Indian filing 7440/DELNP/2015, is already seeking a *Markush* patent encompassing Lenacapavir. This D1/ 7440 application, if granted an Indian patent, shall expire on 28/Feb/2034. Thus, the present application ('277) that carries an international filing date of 17/Aug/2017, is nothing but an ill-founded attempt at extending the monopoly on Lenacapavir compound from Feb 2034 through to Aug 2037. This attempt at extending patent term is not allowed in our statute or jurisprudence.

THAT CLAIMS OF PRESENT APPLICATION ARE NOT AN INVENTION UNDER SECTION 3(e)

65. It is submitted that claims5 and 7-12 of the Present Application are liable to be rejected as the claimed composition is a mere admixture resulting in mere aggregation of properties and not an invention under Section 3(e) of the Patents Act.

66. The Patents Act under Section 3(e) excludes patentability of a substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such substance.

67. It may be noted that while determining the question of a claim passing the test of Section 3(e), Asst. Controller of Patents and Designs had remarked that, "*The question of efficacy and or synergism are matters of scientific facts which are required to be embodied in the specification so that the said characteristics are apparent from the specification.*" (See order of the Asst. Controller of Patents & Designs in patent application314/MUM/2008, at lines 3-5 at internal page 7).

68. As noted earlier, the Applicant has not given sufficient details for composition– in terms of a working composition anywhere in the

Specification. The disclosure is 'paper thin' and does not explain quantitative details or details pertaining to scaling the formulation. Further the burden is on the Applicant to show synergism by supportive experimental data or comparative examples for disclosed composition versus other compositions. Further, such burden is not discharged by merely indicating the % of each of the ingredients of the composition. (See the order of the Controller in 3725/CHENP/2006at internal page 4. Para 8).

69. It is submitted that compositions claimed in Claims5, 7-12 of the Present Application are a mere admixture. The resulting formulations will have mere aggregation of properties of the individual components. Further, the Applicant has failed to disclose any synergistic effect of the claimed composition in the complete specification. With the failure to fulfill its obligation to provide experimental or comparative data to show synergy of the claimed formulation, the formulation claims 12 fails Section 3(e) and must be rejected.

IV. CLAIMS OF THE PRESENT APPLICATION ARE CHALLENGED UNDER SECTION 25(1)(g) OF THE PATENTS ACT, ON GROUND THAT THE SPECIFCATION DOES NOT SUFFIECIENTLY / CLEARLY DESCRIBE THE INVENTION OR THE METHOD FOR ITS PERFORMANCE.

70. S.25(1)(g) requires that the claims be rejected if the underlying Specification does not sufficiently and clearly describe the invention or the method by which it is to be performed.

71. Present Specification does not give complete/ relevant details for specific long acting formulation beyond giving superficial details in the 'formulation example' along the lines of '*A suspension of a compound of Formula Ib in 2% poloxamer 188 in saline (200mg/mL) was prepared*' for administering to dogs- on a laboratory scale. Going further, the last segment of the example discusses making an *in-situ* sodium salt of compound Ib with NaOH in the

solution. The examples do not give any specifics on how such formulations (in terms of quantity) were actually prepared or how can such formulations be prepared on industrial scale.

72. Accordingly, the Specification does not give clear and precise guidance for making long acting injectable formulations of claims 5, 7-12 and hence these claims are liable for rejection under S.25(1)(g).

PRAYER FOR RELIEF

73. In view of the above said references Opponent prays as follows:

a) To be heard and be allowed to lead evidence (documentary and oral) before any order is passed;

b) To reject the claims of Application No. 201917006277*in toto*;

c) To allow the Opponent to file further documents as evidence if necessary to support the averments;

d) To allow amendment of the opposition as and when the need may arise;

e) To allow the Opponent to make further submissions in case the Applicant amends the claims;

f) For costs in this matter;

g) For any further and other relief in the facts and circumstances that may be granted in favour of the Opponent in the interest of justice.

Dated this day 08thof April, 2021

RAJESHWARI H IN/PA - 0358
AGENT FOR THE OPPONENT
OF RAJESHWARI AND ASSOCIATES

To,
The Controller of Patents
The Patent Office, Delhi

INDIA NON JUDICIAL

Government of National Capital Territory of Delhi

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FORM 26
THE PATENTS ACT, 1970
(39 of 1970)
&
The Patent Rules, 2003
FORM OF AUTHORISATION OF A PATENT AGENT/OR ANY PERSON IN A MATTER OR PROCEEDING UNDER THE ACT
[See sections 127 and 132 and rule 135]

We, **THE DELHI NETWORK OF POSITIVE PEOPLE**, having its office at A1-5, House No. 141 Gali No. 3, IGNOU Main Road, Neb Saral, New Delhi - 110068; hereby authorize Rajeshwari H., Gopalan Deepak Sriniwas, Sweety Sharma, Pragya Singh Thakur and Lata Tiwari, all Indian citizens, Advocates / Patent Agents of RAJESHWARI & ASSOCIATES, A – 202, FIRST FLOOR, SHIVALIK ENCLAVE, MALVIYA NAGAR, NEW DELHI - 110017, INDIA, jointly or severally to act on our behalf for filing an opposition and/or representation by the way of opposition against the Indian Patent Application No.: 201917006277 filed on 18/02/2019 by GILEAD SCIENCES, INC. entitled: "**THERAPEUTIC COMPOUNDS USEFUL FOR THE PROPHYLACTIC OR THERAPEUTIC TREATMENT OF AN HIV VIRUS INFECTION"** is a National Phase of PCT Application No. PCT/US2017/047416 dated 17/08/2017 under the above mentioned Act and in all matters and proceedings relating to the patent applications before the Controller of Patents or the Government of India in connection therewith or incidental thereto and in general to do all acts or things including filing of representation, statements, replies, extensions, fees, evidence and any or all documents or pleadings, attending hearings and appointment of a substitute or substitutes as the said Agent(s) may deem necessary or expedient and request that all notices, requisitions and communication relating thereto may be sent to such Agent(s) at Rajeshwari & Associates, India.

We hereby revoke all previous authorization, if any made, in respect of same matter or proceeding.

We hereby assent to the action already taken by the said person in the above matter.

Dated this 08th day of April, 2021

(Shri Jai Prakash)
President
Signature:

The Delhi Network of Positive People
Delhi

To
The Controller of Patents
The Patent Office, New Delhi