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GNA/AF/069/17-18

1st November, 2017

To,
The Controller of Patents
The Patent Office,
Government of India,
Boudhik Sampada Bhavan,
Plot No. 32, Sector-14, Dwarka,
New Delhi – 110075

Dear Sir,

Sub: Pre-grant Representation/Opposition to the Patent Application
under Section 25(1) of the Patents Act, 1970 and Rule 55(1) of the
Patents Rules, 2003 (amended upto 2014)

Reg: Patent Application No. 4351/DELNP/2013A published under
Section 11A on 17th June, 2016.

We are filing this Pre-grant representation/Opposition under Section 25(1) of the
Patents Act, 1970 read with Rule 55(1) of the Patents Rule, 2003 on Form-7A. The
Written Statement and evidence (attached herewith as Exhibits) are enclosed
herewith in duplicate.

As per provision of the Patent Act, 1970, we are entitled to file this Pre-grant
Opposition any-time before grant of patent. As per the status available under
inPASS, the Official website of the Indian Patent Office, the Application is Awaiting
Examination.
This pre-grant opposition is being filed by us on behalf of Mr. Eldred Tellis. We request you to take this Pre-grant Opposition on record and process the same accordingly.

We further request you to provide us a copy of the Reply Statement and evidence and further claim amendments, if any, filed by Patent Applicant. We also request you to grant us a personal hearing under Rule 55(1).

Also, please find enclosed herewith Form 26 (Power of Attorney), in original.

Thanking you in anticipation.

Kindly acknowledge receipt.

With best regards,

Dr. Gopakumar G. Nair
Regn. No: IN/PA 509
Gopakumar Nair Associates
Encl.: as above

C.C: K & S Partners
Intellectual Property Attorneys
109, Sector – 44, Gurgaon – 122 003
National Capital Region, India.
Tel.: +91 (124) 4708 700
FORM 26

THE PATENT ACT, 1970
(39 of 1970)

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]

I, Mr. Eldred Tellis, Indian inhabitant, residing at 115, Belle Vue, Dr. Ambedkar Road, Pali Hill, Bandra West, Mumbai 400 050, India, hereby authorize Ms. Veena Johari, Advocate, Courtyard Attorneys, Ms. Julie George, Advocate, and Dr. Gopakumar G. Nair, Dr. Aruna Sree, Ms. Andreya Fernandes and Ms. Kavita Rao Parmar, of Gopakumar Nair Associates having office at 3rd Floor, ‘Shivmangal’, Akurlur Road, Kandivali (East), Mumbai – 400 101, Maharashtra, India, all Indian inhabitants, to act jointly and severally on my behalf in connection with

I request that all notices, requisition and communication relating thereto may be sent to such persons at the above address unless otherwise specified.

I hereby revoke all previous authorisation, if any, made in respect of the same matter or proceedings.

I hereby assent to the action already taken by the said persons in the above matter.

Dated this 29th day of September 2017

Mr. Eldred Tellis

To
The Controller of Patents
The Patent Office
At Delhi

BEFORE ME
S. K. TAMBAWALLA
ADVOCATE, HIGH COURT
B-23, Tekhem Manzil
Nesbitt Road, Marine
Mumbai - 400 010

29, 9, 17

NOTARY & REGISTERED
276 29 29, 9, 17
FORM 7-A
AND
THE PATENTS RULES, 2003
REPRESENTATION FOR OPPOSITION TO GRANT OF PATENT
[Rule 55]

I, Mr. Eldred Tellis, Indian Inhabitant, hereby give representation by way of opposition to the grant of patent in respect of application no. 4351/DELNP/2013 dated 15th May, 2013 made by Gilead Pharmasset LLC (Gilead Pharmasset LLC) and published on 17th June, 2016 on the grounds of

1. Section 25(1)(b),
2. Section 25(1)(e) and
3. Section 25(1)(f)

Our address for service in India is
Gopakumar Nair Associates
3rd floor, Shivmangal, Next to Big Bazaar,
Akurli Road, Kandivli (East), Mumbai-400101
Maharashtra, India. Phone: 91-22-40895454
E-mail: gopanair@gnaipr.net

Dated this 1st day of November, 2017

Dr. Gopakumar G. Nair
(Reg No. IN/PA 509)
(Agent for the Opponent)
Gopakumar Nair Associates

To
The Controller of Patents,
The Patent Office, At Delhi
STATEMENT OF FACTS/ EVIDENCE

1. The Opponent is an adult Indian citizen. He is a social worker and, since 1983, has been working in the field of public health
especially with drug users including injecting drug users, who are particularly vulnerable to infection with Human Immuno-deficiency virus (hereinafter referred to as “HIV”) and Hepatitis C virus (hereinafter referred to as “HCV”). He is the Executive Director of Sankalp Rehabilitation Trust which provides care and treatment services to drug users. He is also presently the President of the Western Harm Reduction Network, a network of organisations and professionals who work with drug users and provide care and treatment to drug users and also work on issues pertaining to HIV and HCV. The Opponent hereby makes a representation by way of opposition against the grant of patent application, presently titled “Condensed Imidazolylimidazoles as antiviral compounds” bearing Indian Patent Application No. 4351/DELNP/2013 (hereinafter referred to as “the present Application”) filed by Gilead Sciences, Inc. and now being prosecuted by Gilead Pharmasset LLC (hereinafter referred to as “Patent Applicant”), having its office at 333 Lakeside Drive, Foster City, CA 94404, United States of America.

The Opponent submits as follows.

2. The representation by way of opposition is being filed on Form-7A under section 25(1) of the Patents Act, 1970 as amended by the Patents (Amendment) Act, 2005 (hereinafter referred to as “the Patents Act”) and Rule 55 of the Patents Rules, 2003 as amended by the Patents (Amendment) Rules, 2016. Any submission made or evidence adduced with specific reference to any clause of section 25(1) may be treated as being made without prejudice to other submissions made elsewhere in this representation by way of
opposition or any other opposition proceeding before the Indian Patent Office.

3. The Opponent submits that he is opposing the grant of a patent to the present Application reciting Claims 1 to 6 by availing strong and valid grounds provided under Section 25(1) of the Patents Act and is consequently filing the present representation by way of opposition to the present Application.

I. LOCUS STANDI

4. Representation by way of opposition can be made by any person in writing under section 25(1) of the Patents Act. Notwithstanding this, the Opponent submits that he is a “person interested” under section 2(1)(t) in the field of the present invention and has locus standi to initiate the present representation by way of opposition. As stated above, the Opponent has been working with drug users, including injecting drug users, since 1983. Because of the vulnerability of injecting drug users to HIV, the Opponent started working on issues relating to drug users and HIV in or around 1989. On becoming aware of the vulnerability of injecting drug users to HCV and the infection of several of the drug users he knew with HCV, he started working on issues relating to HCV in or around 2003. A large percentage of the drug users that the Opponent works with and knows are infected with HCV and need treatment for the same. Governments of very few states in India provide treatment for HCV. Patients who are infected with HCV and who need treatment have to purchase the treatment on their own. Thus, being a person who is actively involved in providing care and treatment to injecting drug users, a large percentage of
whom are infected with HCV and in need of treatment for the same, and as one who is actively engaged in advocacy on these issues, the Opponent has a real and substantial interest in the aforesaid patent application being opposed.

II. JURISDICTION

5. The present Application has been filed by the Patent Applicant at the Patent Office in Delhi. Therefore, the Patent Controller has the jurisdiction to hear this representation by way of opposition in Delhi.

III. BACKGROUND

6. Discovered in 1989, Hepatitis C is a contagious disease which is caused by a virus, HCV, that infects the liver. If left untreated, Hepatitis C can lead to liver cancer, liver damage and ultimately liver failure.

7. The present Application claims a patent over a molecule to treat HCV. It claims the molecule, its pharmaceutically acceptable salts, a pharmaceutical composition thereof and a composition further comprising a Hepatitis C NS5B polymerase inhibitor.

8. As initially filed, the present Application claimed several molecules. However, as amended, the claims are restricted primarily to a single molecule now identified as velpatasvir, and its combination with an inhibitor of Hepatitis C NS5B polymerase. Velpatasvir is presently approved for use in combination with sofosbuvir, a Hepatitis C NS5B polymerase, for patients infected with HCV.
9. *Velpatasvir* is a pentacyclic, imidazole containing NS5A inhibitor to treat HCV. As shown below, NS5A inhibition had been identified as a promising target for HCV treatment. The use of pentacyclic agents as well as imidazole containing agents in antiviral therapy was also known well before the priority date.

**NS5A known and used for treatment of HCV**


13. One such NS5A inhibitor under development was BMS-790052, which was at that time identified to be the most potent HCV inhibitor. It was reported as being highly effective against genotype 1 replicons, displaying robust genotype 1 anti-HCV activity in the clinic and displaying promising inhibition of genotype 2a JFH1 replicon cells and cell culture infectious virus [Fridell, et al., “Distinct functions of NS5A in Hepatitis C Virus RNA Replication Uncovered by Studies with the NS5A Inhibitor BMS-790052” (2011) Journal of Virology 85(14): 7312–20].

14. Thus HCV NS5A had already been identified as a target for development of drugs to treat HCV.
Polycyclic compounds and imidazole known for decades

15. Polycyclic compounds were known to possess a variety of biological activities. For example, potent antiviral activity of naturally occurring photosensitizer hypericin had been known for over a decade [Carpenter, et al., “Chemiluminescent activation of the antiviral activity of hypericin: a molecular flashlight” (1994) *Proceedings of the National Academy of Sciences of the United States of America* 91:12273–77]. Also, pentacyclic structures such as triterpenes were known to have a wide spectrum of biological activities and some usefulness in medicine. The antiviral properties of one such triterpene, betulinic acid, had also been confirmed in clinical trials more than a decade ago [Patočka, “Biologically active pentacyclic triterpenes and their current medicine signification” (2003) *Journal of Applied Biomedicine* 1:7–12].

16. Drugs containing imidazole were known to have a broad scope in clinical medicines because of the therapeutic properties of imidazole. Imidazole is an organic compound with the formula (CH)₂N(NH)CH. In chemistry, it is an aromatic heterocycle, classified as a diazole and as an alkaloid. Imidazoles are a common component of a large number of natural products, such as purine, histamine and histidine. In the 19th century, imidazole was synthesised and various imidazole derivatives were discovered. Due to its therapeutic properties, imidazole was also incorporated in drugs to synthesise pharmacologically active molecules. Imidazole and its derivatives were reported to be physiologically and pharmacologically active and found applications in the

**Impact of patent on treatment for Hepatitis C**

17. According to the WHO Global Hepatitis Report 2017, in 2015, an estimated 71 million people were living with chronic HCV infection and an estimated 1.75 million new HCV infections occurred worldwide in 2015.

18. While accurate figures are not available due to the absence of appropriate surveillance, it is estimated that, as of 2015, India has a population prevalence of around one per cent of Hepatitis C infection [World Health Organization, “Hepatitis C Fact Sheet – July 2015].

19. The situation with respect to access to treatment for Hepatitis C is quite alarming. As noted by the WHO in the Global Hepatitis Report 2017, access to affordable hepatitis testing is limited; only 20 per cent of people with viral HCV have been diagnosed. Even amongst those diagnosed, treatment has reached only a small fraction. In 2015, only 7.4 per cent of those diagnosed with HCV infection, i.e. 1.1 million persons, had commenced treatment. Of the cumulative 5.5 million people who were on treatment for HCV
in 2015, only about half a million of these persons had received the more recently approved and better-tolerated class of direct-acting antivirals (hereinafter referred to as “DAAs”). In fact, the WHO notes that there were more new HCV infections than patients who were started on treatment.

20. There is clearly a great need for DAAs to be made more widely available to those who are infected with HCV. For this it is important that the drugs are affordable and available widely to everyone.

21. It is known that patents impose barriers to affordability, accessibility and availability of medicines. Therefore, patents ought to be granted only for truly deserving applications which meet the high patentability standards of “newness” and inventive step. Granting patents to non-novel compounds or compounds that are developed as a result of routine improvements in the pharmaceutical field create barriers in access to medicines.

22. As will be shown below, velpatasvir was already in the public domain. The Patent Applicant is now seeking to obtain a patent over this known compound and its salt form and some pharmaceutical compositions thereof.

23. Given that there is no patent in India covering velpatasvir, if a patent is granted the Patent Applicant will obtain a monopoly over velpatasvir until about November 2032. Velpatasvir has been approved to be used in combination with sofosbuvir (100 mg + 400 mg, respectively). In the United States of America, it is sold at a
price of approximately USD 74,760 for the 12-week treatment. In India, it appears that several pharmaceutical companies have been licensed by the Patent Applicant to sell this combination. These licensees are selling the combination for approximately Rs.18,500/- for 28 tablets, i.e. approximately Rs. 660/- per tablet and approximately Rs. 55,500/- for the prescribed 84-days’ treatment. The cost charged by the multiple Indian licensees of the Patent Applicant is not competitive and out of reach of the masses who require the treatment. If a patent is granted, the likelihood of a further lowering of the prices due to unrestricted competition between multiple players will be impeded.

24. Given the estimated prevalence of Hepatitis C in India, it is essential that drugs for treating it should be made available at competitive and low prices so that people are able to avail of treatment at affordable rates.

25. The Opponent states that the right to health guaranteed under Article 21 of the Constitution of India is paramount and that the medicines required for Hepatitis C treatment ought to be made available at affordable and low costs, so that the maximum people can benefit from the treatment, and lives can be saved. The wrongful grant of a patent to the Patent Applicant would be a breach of the fundamental right to health of a large number of patients with Hepatitis C who ought to be able to obtain medicines at competitive prices and not monopolistic prices.

26. As will be shown below, the alleged invention is not new and lacks inventive step and does not meet the standards of invention or
The patentability set out under the Indian patent law. Therefore, the claims of the present Application ought to be rejected *in toto*.

**IV. PATENT APPLICANT’S CONTENTION**

27. The present Application was filed in India on 15 May 2013 and published in India on 17 June 2016. As originally filed, the present Application had 42 claims. On or about 16 February 2015, the Patent Applicant filed an application seeking to amend the claims. As of today, the Patent Applicant is pursuing six claims. The bibliographic page along with ‘as filed’ and ‘amended’ claims of the present Application, as retrieved from the website of the Indian Patent Office website, is enclosed herewith as **Exhibit 1**.

28. The claims of the present Application relate to methyl \{(2S)-1-[(2S,5S)-2-(9-{2-[(2S,4S)-1-{(2R)-2-[(methoxycarbonyl)amino]-2-phenylacetyl}-4-(methoxymethyl)pyrrolidin-2-yl]-1H-imidazol-5-yl}-1,11-dihydroisochromeno[4’,3’:6,7]naphtho[1,2-d]imidazol-2-yl]-5-methylpyrrolidin-1-yl]-3-methyl-1-oxobutan-2-yl\} carbamate. This compound is now identified as **velpatasvir**.

29. The present Application is the national phase entry of PCT Application No. PCT/US2012/065681 (hereinafter referred to as the “present Application”) which was published as WO 2013/075029. This PCT application was filed on 16 November 2012, claiming a priority of 16 November 2011. The complete specification WO 2013/075029 as retrieved from the website of the WIPO, is enclosed herewith as **Exhibit 2**.
V. SUMMARY OF CLAIMS

30. The claims as amended on or about 16 February 2015 are tabulated below for comparison:

<table>
<thead>
<tr>
<th>Claim 1 relates to</th>
<th>Claim 4 relates to</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Chemical Structure" /></td>
<td><img src="image2" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>or a pharmaceutically acceptable salt thereof</td>
<td>or a pharmaceutically acceptable salt thereof</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Claim 2 depends on Claim 1 and claims a pharmaceutical composition comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.</th>
<th>Claim 5 depends on Claim 4 and claims a pharmaceutical composition comprising the compound of Claim 4 and a pharmaceutically acceptable carrier.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3" alt="Chemical Structure" /></td>
<td><img src="image4" alt="Chemical Structure" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Claim 3 depends on Claim 2 and claims such a pharmaceutical composition further comprising a NS5B polymerase inhibitor.</th>
<th>Claim 6 depends on Claim 5 and claims such a pharmaceutical composition further comprising a NS5B polymerase inhibitor.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image5" alt="Chemical Structure" /></td>
<td><img src="image6" alt="Chemical Structure" /></td>
</tr>
</tbody>
</table>

31. As seen from the table, Claim 1 and Claim 4 claim the same compound, *velpatasvir*. The only difference is that Claim 1 includes a pharmaceutically acceptable salt of *velpatasvir* too while
Claim 4 relates to velpatasvir only. Therefore, Claim 4 is covered by Claim 1.

32. Claim 2 relates to a pharmaceutical composition comprising the compound of Claim 1 (velpatasvir or its pharmaceutically acceptable salt) and a pharmaceutically acceptable carrier. Similarly, Claim 5 relates to a pharmaceutical composition comprising the compound of Claim 4 (velpatasvir) and a pharmaceutically acceptable carrier. Therefore, Claim 5 is covered by Claim 2.

33. Claim 3 depends on Claim 2 and claims such a pharmaceutical composition further comprising a NS5B polymerase inhibitor. Similarly, Claim 6 depends on Claim 5 and claims such a pharmaceutical composition further comprising a NS5B polymerase inhibitor. Therefore, Claim 6 is covered by Claim 3.

VI. PRE-GRANT OPPOSITION ON THE FOLLOWING GROUNDS

34. Section 25(1): Opposition to the patent where the application has been published but not granted. The following grounds and evidence sets out the basis of the opposition to the present Application.

35. It is submitted that the alleged invention claimed in the present Application is not an invention within the meaning of section 2(1)(j) of the Patents Act, is not new, does not involve an inventive step as defined under section 2(1)(ja) of the Patents Act, is not a new invention as defined under section 2(1)(l) of the Patents Act as it has been anticipated by prior publication and is not patentable
under section 3(d) of the Patents Act (which disallows patenting of new forms, including derivatives, salts and combinations, of known substances) and section 3(e) of the Patents Act (which disallows patenting of a substance obtained by mere admixture).

36. The Opponent is filing this pre-grant opposition availing several of the grounds set out in section 25(1) of the Patents Act. The primary grounds of pre-grant opposition, which are raised without prejudice to one another, are: (i) Section 25(1)(b)—that the invention so far claimed has been published before the priority date of the claim; (ii) Section 25(1)(e)—that the invention so claimed is obvious and clearly does not involve an inventive step and (iii) Section 25(1)(f)—that the subject of any claim is not an invention within the meaning of this Act and is not patentable under this Act.

37. The following documents filed herewith provide evidence in support of the grounds of opposition:
   (a) **Exhibit 3**: PubChem database of February 2011 disclosing velpatasvir;
   (b) **Exhibit 4**: WO 2010/132601 titled “Antiviral compounds” filed by Gilead Sciences, Inc. and published on 18 November 2010;
   (c) **Exhibit 5**: WO 2010/111534 titled “Fused ring inhibitors of Hepatitis C” filed by Presidio Pharmaceuticals, Inc. and published on 30 September 2010;
   (d) **Exhibit 6**: WO 2005/082880 titled “Dibenzochromene derivatives and their use as ERβ selective ligands” filed by Wyeth and published on 9 September 2005;
(e) **Exhibit 7:** WO 2009/102325 titled “Imidazolyl biphenyl imidazole as hepatitis C inhibitors” filed by Bristol-Myers Squibb Company and published on 20 August 2009; and  
(f) **Exhibit 8:** WO 2012/068234 titled “Antiviral compounds” filed by Gilead Sciences, Inc. and published on 24 May 2012.

38. The Opponent states that none of the claims filed by the Patent Applicant should be deemed accepted, unless the same are specifically admitted / accepted herein, and that the Opponent opposes all the claims filed by the Patent Applicant as amended on 16 February 2015.

39. For reasons set out in detail below, the claims of the present Application for *velpatasvir* and / or its salts, pharmaceutical compositions thereof and combinations are not patentable under the Act, and the present Application should be rejected in toto.

**VI.A. SECTION 25(1)(b): NOT NEW AND ANTICIPATION BY PRIOR PUBLICATION**  
(i) Section 25(1)(b) provides a ground of opposition on the ground, *inter alia*, that the invention so far as claimed in a claim of complete specification has been published before the priority date of the claim in India or elsewhere, in any other document.
Claims 1 to 6 are not new and are anticipated by the disclosures in public databases

(ii) The claims of the present Application are anticipated by publication by the disclosures in public databases.

(iii) An entry on PubChem<https://pubchem.ncbi.nlm.nih.gov/>, a database for chemical molecules maintained by the United States National Center for Biotechnology Information, for a compound identified as CHEBI:133009 shows that a molecule having the following structure was available on 10 February 2011 on PubChem. According to the entry, CHEBI:133009 was first made available on PubChem on 19 November 2009. A pdf print-out of the entry is enclosed hereto as “Exhibit 3”. *Ex facie*, prior to the priority date of the present Application, the molecule available at least as of 10 February 2011 is identical to the compound claimed in Claims 1 and 4.

(iv) Admittedly, the PubChem entry for CHEBI:133009 discloses four versions. Versions 1 and 2 were made available prior to the priority date, while versions 3 and 4 were made available after the priority date.
(v) The structure available on 19 November 2009 for version 1 reveals a structure of the claimed compounds, even though at first glance it may not appear to be so.

(vi) The structure entry for version 2 of the molecule identified as CHEBI:133009, hereinabove, which was available as on 10 February 2011, is that of the claimed compound, velpatasvir.

(vii) Therefore, at the very least, version 2 of the said PubChem entry anticipates and describes the claimed compound.

(viii) It may be noted that from the records it appears that the entry was removed by ChEBI from its database as part of a release. Nonetheless, it appears to have continued to remain available online on PubChem and was modified on 10 February 2011.

(ix) The fact that the compound was available at any point of time before the priority date to the administrators of ChEBI and PubChem and was available on their websites and as part of ChEBI’s release to the public, means that it was already disclosed to the public by publication.

(x) Thus, the compound as claimed in Claims 1 and 4 is disclosed and anticipated by prior publication and forms part of the prior art and is not new. Therefore, Claims 1 and 4 ought to be rejected in toto.

(xi) As Claims 2, 3, 5 and 6 are dependent on Claims 1 and 4, they too ought to be rejected.
As set out above, Claims 1 to 6, and more particularly, Claims 1 and 4, of the present Application are anticipated by prior publication by the disclosures of Exhibit 3 and ought to be rejected under section 2(1)(j) read with section 25(1)(b) of the Patents Act.

VI.B. SECTION 25(1)(e): OBVIOUSNESS AND LACK OF INVENTIVE STEP

(i) Section 25(1)(e) provides a ground of opposition on the ground that the invention so far is claimed in a claim of complete specification is obvious and clearly does not involve any inventive step, having regard to the matter published, inter alia, in India or elsewhere in any other document.

(ii) Section 2(1)(ja) defines inventive step thus: “‘inventive step’ means a feature of an invention that involves technical advance as compared to existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art” (emphasis supplied).

(iii) Thus, to possess inventive step, the invention must have a feature that (i) involves technical advance as compared to existing knowledge and (ii) is not obvious to a person skilled in the art. It is an established position of law that both these elements set out in the definition of “inventive step” have to be satisfied.

(iv) As stated in the background above, polycyclic molecules to treat HCV were already known.
(v) Without prejudice to anything stated hereinabove, as shown below, Claims 1 to 6 are obvious to a person skilled in the art, do not involve any technical advance and therefore lack inventive step.

Claims 1 to 6 are obvious to a person skilled in the art in light of the disclosures contained in WO ’601

(vi) WO 2010/132601 titled “Antiviral compounds” published on 18 November 2010 (hereinafter referred to as “WO ’601”), a copy of which is enclosed hereto as “Exhibit 4”, discloses imidazole containing polycyclic compounds, amongst other compounds, antiviral compounds and compositions for the treatment of HCV.

(vii) A representative example of this class is as depicted in the following structure, i.e. Compound KC [Exhibit 4, WO ’601, page 911]:

(viii) The structure of compound KC is structurally similar to the claimed compound, velpatasvir, with a central polycyclic core attached to an imidazole ring on either side which is in turn substituted with peptide type side chain. This specific compound exhibits very good potency for anti-HCV activity (EC50 of 0.0044 nM; Exhibit 4, WO ’601, page 965, row 3).
(ix) The minor structural differences between velpatasvir and the above compound KC include a dibenzochromene core in example KC instead of a dihydroisochromeno-naphto-imidazolyl present in velpatasvir and modification of substitutions in the peptide side chains.

(x) With regard to the differences in the core, as seen in the following figure, the first difference is fusion of the imidazole ring to the tetracyclic core which is 6$H$-dibenzo[c,h] chromene for KC and 5$H$-dibenzo[c,g] chromene in case of velpatasvir, which are structural congeners.

(xi) With respect to the peptide side chain, velpatasvir contains a phenyl group on the left hand peptide side chain with a methoxymethyl group attached to the pyrrolidine ring of this peptide side chain and an isopropyl group on the right hand peptide side chain with a methyl group attached to the pyrrolidine ring of this peptide side chain, while compound KC has isopropyl groups on both peptide-type side chains with pyrrolidine rings being unsubstituted.
(xii) A similar derivative KD includes the same core structure as derivative KC with phenyl substitution on both the peptide side chains [Exhibit 4, WO ’601, page 913]. This compound too exhibits very good potency for anti-HCV activity (EC₅₀ of 0.0275 nM; Exhibit 4, WO ’601, page 972, row 5).

(xiii) Another structure described in WO ’601 exhibits side chain substitution identical to velpatasvir, i.e. phenyl on the left hand peptide side chain and isopropyl on the right hand peptide side chain. This structure has a phenylnaphthylene core (represented in big red circle in the centre of the following figure) instead of dibenzochromene (represented in red circle on the right hand side in the following image), which can be considered as a fusion of the naphthyl and phenyl rings with an oxygen and methyl carbon linkage. (EC₅₀ of 0.0083 nM; Exhibit 4, WO ’601, page 974, row 1)

(xiv) WO ’601 also discloses the potency for several structurally similar compounds. A close study of the structures and modifications thereto reveals a trend in the change in potency of the molecules upon the modification of the core when the side chains are
constant. Each of the examples included in the table below contains (i) a core containing six member ring having either one or more rings which are separate or fused, (ii) either one imidazole group or two imidazole groups one on either side of the core and (iii) an isopropyl substituted peptide side-chain on either side. The compounds have been tested using a common assay protocol. Therefore, the potency comparison will give a fair idea about the structure activity relationship.

<table>
<thead>
<tr>
<th>No.</th>
<th>Structure</th>
<th>Description</th>
<th>EC$_{50}$ value</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td><img src="image1" alt="Non-fused core" /></td>
<td>Non-fused core</td>
<td>1.2200 nM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>WO’ 601, page 920, last row</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td><img src="image2" alt="Phenyl ring added to core" /></td>
<td>Phenyl ring added to core</td>
<td>0.0719 nM</td>
<td>Addition of a phenyl ring to Structure I results in improved potency.</td>
</tr>
<tr>
<td></td>
<td>WO’ 601, page 940, second row</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III.</td>
<td><img src="image3" alt="Imidazole ring removed from right hand side of compound" /></td>
<td>Imidazole ring removed from right hand side of</td>
<td>1.4010 nM</td>
<td>Removal of imidazole ring from compound results in unfavourab</td>
</tr>
<tr>
<td>No.</td>
<td>Structure</td>
<td>Description</td>
<td>EC&lt;sub&gt;50&lt;/sub&gt; value</td>
<td>Comment</td>
</tr>
<tr>
<td>-----</td>
<td>-----------</td>
<td>-------------</td>
<td>----------------------</td>
<td>---------</td>
</tr>
<tr>
<td>IV</td>
<td><img src="image" alt="Right hand side imidazole ring fused to the phenyl ring" /></td>
<td>molecule and amide containing aliphatic side chain added</td>
<td>0.0372 nM</td>
<td>Fusing the right hand side imidazole ring fused to the phenyl ring shows many fold improvement in potency.</td>
</tr>
<tr>
<td>V.</td>
<td><img src="image" alt="Both imidazole rings fused" /></td>
<td>Both imidazole rings fused</td>
<td>35.467 3 nM</td>
<td>Fusing both the imidazole rings fused</td>
</tr>
<tr>
<td>No.</td>
<td>Structure</td>
<td>Description</td>
<td>EC$_{50}$ value</td>
<td>Comment</td>
</tr>
<tr>
<td>-----</td>
<td>------------</td>
<td>-------------</td>
<td>-----------------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td>WO’ 601, page 926, fourth row</td>
<td>Biphenyl core modified to napthyl core</td>
<td>0.0511 nM</td>
<td>Modifying the biphenyl core to a naphthyl (fused) core shows improvement in potency as compared to the phenyl (Structure I) or the biphenyl (Structure II) core.</td>
</tr>
<tr>
<td></td>
<td>WO’ 601, page 928, fourth row</td>
<td>to the biphenyl core</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Structure</td>
<td>Description</td>
<td>EC&lt;sub&gt;50&lt;/sub&gt; value</td>
<td>Comment</td>
</tr>
<tr>
<td>-----</td>
<td>-----------</td>
<td>-------------</td>
<td>-----------------------</td>
<td>---------</td>
</tr>
<tr>
<td>VII.</td>
<td><img src="image1.png" alt="Structure" /></td>
<td>Right hand side imidazole ring fused to the right hand side phenyl ring</td>
<td>0.0054 nM</td>
<td>Adding a phenyl ring to the core and fusing the right hand side imidazole ring to the phenyl ring shows many fold improvement in potency compared to Structure I and Structure IV.</td>
</tr>
<tr>
<td>VIII.</td>
<td><img src="image2.png" alt="Structure" /></td>
<td>Removal of imidazole ring from the right hand side of</td>
<td>0.0111 nM</td>
<td>Removing the imidazole ring from the right hand side of Structure</td>
</tr>
<tr>
<td>No.</td>
<td>Structure</td>
<td>Description</td>
<td>EC$_{50}$ value</td>
<td>Comment</td>
</tr>
<tr>
<td>-----</td>
<td>-----------</td>
<td>-------------</td>
<td>----------------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Structure VII. (The point of attachment of the side chain to the right hand side terminal phenyl ring is meta with respect to the central core)</td>
<td></td>
<td>VII causes few fold loss of potency.</td>
</tr>
<tr>
<td>IX.</td>
<td><img src="image1.png" alt="Image" /></td>
<td>Removal of imidazole ring from the right hand side of Structure VII. (The point of attachment</td>
<td>0.0875 nM</td>
<td>Removing the imidazole ring from the right hand side of Structure VII causes few fold loss of potency.</td>
</tr>
<tr>
<td></td>
<td>WO’ 601, page 931, row 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Structure</td>
<td>Description</td>
<td>EC$_{50}$ value</td>
<td>Comment</td>
</tr>
<tr>
<td>-----</td>
<td>-----------</td>
<td>-------------</td>
<td>----------------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td><img src="image" alt="Structure" /></td>
<td>of the side chain to the right hand side terminal phenyl ring is meta with respect to the central core)</td>
<td>0.0131 nM</td>
<td>Converting the biphenyl core of Structure II to a polycyclic core having oxygen containing six membered ring improves potency</td>
</tr>
</tbody>
</table>

WO’ 601, page 941, second row
<table>
<thead>
<tr>
<th>No.</th>
<th>Structure</th>
<th>Description</th>
<th>EC$_{50}$ value</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="image1.png" alt="Structure XI" /></td>
<td>Conversion of the core to polycyclic core</td>
<td>0.0044 nM</td>
<td>Converting the central core to a fused polycyclic core having oxygen and increasing the number of rings in the core improved potency of this structure compared to Structure X.</td>
</tr>
<tr>
<td>XI.</td>
<td>WO’ 601, page 965, third row</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><img src="image2.png" alt="Structure XII" /></td>
<td>Partially polycyclic core</td>
<td>0.0037 nM</td>
<td>Partial polycyclic core with fused</td>
</tr>
<tr>
<td>No.</td>
<td>Structure</td>
<td>Description</td>
<td>EC$_{50}$ value</td>
<td>Comment</td>
</tr>
<tr>
<td>-----</td>
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<td>-------------</td>
<td>-----------------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>imidazole ring on the right hand phenyl ring shows better potency than Structure X.</td>
</tr>
</tbody>
</table>

(xv) This data is indicative of the enhanced potency of derivatives with fused core structure with greater number of rings in the core and imidazole ring fused to the core on the right hand side of the core.

(xvi) WO ’601 already discloses polycyclic ring core, more particularly a tetracyclic ring, exhibiting promising potency. It may be noted that the move towards heterocyclic structures is known to allow for more flexible substitution patterns. The advantage of fusing rings to enhance potency is also known in chemistry and is thus not a new discovery or invention. The data from the table above showing the trend in potency demonstrates the advantage of fusing rings in the core and of further fusing this core on the right hand side to an imidazole ring, thereby displaying the expected improvement of potency. It would thus be obvious to a person skilled in the art to modify further fusing the dibenzochromene.
core (of Compound KC) to an imidazole ring on the right hand side.

(xvii) Substitutions on the pyrrolidine ring at the specific position as that of *velpatasvir* have already been explored in WO ’601 (marked in green circle on the left and blue circle on the right in the following figure). Alkyl substitutions such as methyl substitutions are routinely done on heterocyclic ring to probe the effect on activity. Further, a methoxymethyl substitution in the pyrrolidine ring has already been explored in WO ’601. Example GZ shows a methoxymethyl substitution (marked in green circle on the left in the following figure) [Exhibit 4, WO ’601, page 801].

![Diagram of GZ](image)

**GZ**

(xviii) A modification made to derive the structure of *velpatasvir* is to fuse the tricyclic core and imidazole portion (such as that found in example KC) by removal of the direct bond and optimization of the side arms. WO ’601 itself provides the possibility of such structural modifications which encompass the structure of *velpatasvir*.

(xix) A person skilled in the art would carry out obvious structural modifications of the compounds disclosed in WO ’601 to arrive at the structure of *velpatasvir*. The examples of WO ’601 itself
provide Motivation and Teaching for such modifications to the core ring and fusing of imidazole ring to the central core especially at the right hand side of the polycyclic core.

(xx) A person skilled in the art would be motivated and consider the practical application of this data showing structure-activity relationship and arrive at a core having the imidazole ring fused on the right hand side.

(xxi) The variation in the peptide type side chains is not even a mere routine development or workshop development.

(xxii) Therefore, Claims 1 and 4 are obvious to a person skilled in the art and lack inventive step.

(xxiii) WO ’601 discloses and claims the use of the disclosed compounds, including polycyclic, imidazole-containing compounds, as a prodrug or a pharmaceutically acceptable salt [Exhibit 4, WO ’601, page 2 and page 1086, Claim 161] and pharmaceutical compositions comprising the disclosed compounds and at least one pharmaceutically acceptable carrier [Exhibit 4, WO ’601, pages 21–28, page 1086, Claim 162]. Therefore, Claims 1, 2 and 5 of the present Application are obvious to a person skilled in the art and lack inventive step.

(xxiv) WO ’601 discloses and claims such pharmaceutical compositions further comprising at least one additional therapeutic agent [Exhibit 4, WO ’601, pages 28–31 and page 1086, Claim 165]. Claim 165 further lists such additional therapeutic agents for
treating HCV, including NS5B polymerase inhibitors [Exhibit 4, WO ’601, page 29 and page 1086, Claim 165]. Therefore, Claims 3 and 6 are obvious to a person skilled in the art and lack inventive step.

(xxv) Therefore, Claims 1 to 6 of the present Application are obvious to a person skilled in the art and lack inventive step in light of the prior art disclosures contained in WO ’601 (Exhibit 4).

**Claims 1 to 3 and Claims 5 to 6 are obvious to a person skilled in the art in light of the disclosures contained in Exhibit 3 (PubChem) and WO ’601 (Exhibit 4)**

(xxvi) As shown above, Exhibit 3 discloses velpatasvir, the compound claimed in Claims 1 and 4 of the present Application.

(xxvii) Further, as stated in paras xxiii to xxiv above, WO ’601 (Exhibit 4) discloses pharmaceutically acceptable salts of polycyclic ringed NS5A inhibitors, compositions thereof and their combination with other agents, including NS5B inhibitors, for treating HCV.

(xxviii) Therefore, Claim 1 to 3 and Claims 5 to 6 are obvious to a person skilled in the art and lack inventive step in light of the disclosures contained in Exhibit 3 read with WO ’601 (Exhibit 4).

**Claims 1 to 6 are obvious to a person skilled in the art in light of the disclosures contained in WO ’534 (Exhibit 5) either read alone or in combination with WO ’601 (Exhibit 4)**

(xxix) WO 2010/111534 titled “Fused ring inhibitors of Hepatitis C” published on 30 September 2010 (hereinafter referred to as “WO
’534”), a copy of which is enclosed hereto as “Exhibit 5”, discloses fused ring inhibitors of HCV.

(xxx) WO ’534 discloses compounds useful for inhibiting HCV, particularly by inhibiting the functions of the NS5A protein of HCV.

(xxi) WO ’534 describes polycyclic inhibitors of HCV. It also exemplifies at least two compounds having a pentacyclic core resembling that found in velpatasvir [Exhibit 5, WO ’534, page 154, compounds 102 and 103].

(xxii) One of these pentacyclic compounds, which has a core almost identical to the claimed compound, is given below [Exhibit 5, WO ’534, page 154, compound 102]:

![Chemical Structure](image)

The only difference in the core is the arrangement of the rings in relation to each other; however, this is a chemically congeneric arrangement. Compound 102 has a dihydrochroomenonaphtho imidazole while velpatasvir has a dihydroisochromenonaptho imidazole. Such chemical congeners can be expected to exhibit the same activity. The following figure represents the comparison of the core of Compound 102 and velpatasvir.
(xxxiii) In compound 102, the pentacyclic core is attached to an imidazole ring on the left hand side of this core and the two ends so formed have been attached to two substituted peptide type isobutyl side chain.

(xxxiv) WO ’534 also discloses compounds where the peptide type side chains are a combination of different groups. In fact, it also discloses a compound with an isopropyl group (depicted in orange circle on the left in the following figure) on one side chain and phenyl group (depicted in blue circle on the right in the following figure) on the other side chain [Exhibit 5, WO ’534, page 139, compound 15]

This is the same combination of isopropyl group and phenyl group as with velpatasvir, the only difference being that they are attached on opposite sides of the core as compared to velpatasvir.
In light of the disclosures of WO ’534 (Exhibit 5), either alone or in combination with WO ’601 (Exhibit 4), Claims 1 and 4 are obvious to a person skilled in the art and lack inventive step.


Therefore, Claims 1 and 4 and dependent Claims 2 to 3 and 5 to 6 of the present Application are obvious to a person skilled in art and lack inventive step in light of the disclosures contained in WO ’534 (Exhibit 5), either alone or in combination with WO ’601 (Exhibit 4).

**Claims 1 to 6 are obvious to a person skilled in the art in light of the disclosures contained in WO ’880 (Exhibit 6) read in combination with WO ’601 (Exhibit 4) and/or WO ’534 (Exhibit 5)**

WO 2005/082880 titled “Dibenzochromene derivatives and their use as ERβ selective ligands” published on 9 September 2005 (hereinafter referred to as “WO ’880”), a copy of which is enclosed hereto as “Exhibit 6”, discloses compounds with a polycyclic nucleus.

This patent discloses and claims compounds having the following formula [Exhibit 6, WO ’880, pages 4–5]
(xl) These compounds exhibit a structural similarity to *velpatasvir* containing a central polycyclic core nucleus. WO ’880 further discloses the use of these compounds as antioxidants useful in treating or inhibiting free radical induced disease states including viral hepatitis or chronic active hepatitis [*Exhibit 6*, WO ’880, pages 9–10, para [0027]].

(xli) Imidazole ring forms the core of various pharmaceutically active agents and is commonly found in many anti-infective agents.

(xlii) Based on the structure-activity relationship discussion presented above regarding the polycyclic core and the fusion of imidazole ring to the core as disclosed in WO ’601 (*Exhibit 4*) and the pentacyclic core containing imidazole ring disclosed in WO ’534 (*Exhibit 5*), it would have been obvious to a person skilled in art to fuse an imidazole ring to this dibenzochromene core disclosed in WO ’880 (*Exhibit 6*).

(xliii) Therefore, Claims 1 and 4 and dependent Claims 2 to 3 and 5 to 6 are obvious to a person skilled in the art and lack inventive step in light of the disclosures contained in WO ’880 (*Exhibit 6*) read in combination with WO ’601 (*Exhibit 4*) and / or WO ’534 (*Exhibit 5*).
Claims 1 to 6 are obvious to a person skilled in the art in light of the disclosures contained in WO ’325 (Exhibit 7) read in combination with WO ’601 (Exhibit 4) and/or WO ’534 (Exhibit 5)

(xliv) WO 2009/102325 titled “Imidazolyl biphenyl imidazole as hepatitis C inhibitors” published on 20 August 2009 (hereinafter referred to as “WO ’325”), a copy of which is enclosed hereto as “Exhibit 7”, too discloses imidazole-containing biphenyl compounds. It discloses various imidazole containing derivatives or their pharmaceutically acceptable salts or compositions for the treatment of HCV [Exhibit 7, WO ’325, pages 1–29].

(xlv) One such structure which bears a structural similarity to velpatasvir is Compound M151 [Exhibit 7, WO ’325, page 646], which has the following structure:

(xlvi) The structure of Compound M151 has biphenyl as a central core instead of a polycyclic nucleus. It has two peripheral imidazole rings, one on each side. These peripheral rings are substituted with two peptide side chains which are very similar to those found in the structure of velpatasvir. The common peptide side chain parts of the two structures have been marked in green circle on the left and blue circle on the right in the following image and the methyl substitution on the pyrrolidine ring of the peptide side chain common to both these structures has been marked in red circle
(smaller circle within the larger blue circle on the right hand side of each structure) in the following figure.

(xlvii) WO ’325 discloses substitutions on the peptide type side chains which include isopropyl and phenyl groups.

(xlviii) A structurally related compound to compound M151, *daclatasvir* (as depicted in the following image), was approved for use in Europe in 2014 and in the United States of America and India in 2015 for the treatment of HCV.

(xlix) Based on the disclosures contained in WO ’601 (*Exhibit 4*) and / or WO ’534 (*Exhibit 5*) regarding the advantages of a polycyclic fused core, it would have been obvious to a person skilled in art to replace the central biphenyl core with appropriate polycyclic core and arrive at the structure of *velopatasvir*.

(I) On the basis of the disclosures contained in WO ’325 (*Exhibit 7*) read along with the disclosures contained in WO ’601 (*Exhibit 4*)
and / or WO ’534 (Exhibit 5), the compounds claimed in Claims 1 and 4 of the present Application as inhibitors of HCV would have been obvious to a person skilled in art.

(l) WO ’325 further discloses the compositions of and the use of the compounds disclosed therein in combination with other compounds having anti-HCV activity [Exhibit 7, WO ’325, pages 8–9, 20–25 and pages 718–719, claims 3, 4, 8 and 10].

(iii) Therefore, dependent Claims 2 to 3 and Claims 5 to 6 too would have been obvious to a person skilled in the art and lack inventive step.

(iii) Therefore, Claims 1 and 4 and dependent Claims 2 to 3 and Claims 5 to 6 are obvious to a person skilled in the art and lack inventive step in light of the disclosures contained in WO ’325 (Exhibit 7) read in combination with WO ’601 (Exhibit 4) and / or WO ’534 (Exhibit 5).

**Claims 1 to 6 do not involve a technical advance over existing knowledge**

(liv) Given the disclosures contained in Exhibits 3 to 8 above, the alleged invention does not involve a feature that involves a technical advance over existing knowledge.

(lv) The Complete Specification too is silent on this.

(lvi) Therefore, Claims 1 to 6 lack inventive step.
Conclusion

(lvii) Thus, Claims 1 to 6 of the present Application lack inventive step because they are obvious to a person skilled in the art and do not involve a technical advance. They, therefore, ought to be rejected under section 2(1)(ja) read with section 25(1)(e) of the Patents Act.

VI.C. SECTION 25(1)(f): FAILURE TO MEET SECTION 3(d)

(i) Section 25(1)(f) provides a ground of opposition on the ground that the subject of any claim is not an invention within the meaning of the Patents Act or is not patentable under the Patents Act.

(ii) Section 3(d) provides that new forms of known substances are not patentable unless they Exhibit an enhanced efficacy. The explanation to section 3(d) provides that this includes derivatives and combinations of known substances.


(iv) It is also an established position of law that the burden of proof of showing enhanced efficacy, i.e. enhanced therapeutic efficacy, for the claimed compound is on the patent applicant and that the proof of enhanced efficacy is to be part of the complete specification [Novartis AG v. Union of India and Others, (2007) 4 MLJ 1153, at para 13].
(v) As of the priority date, imidazoles and various polycyclic compounds containing imidazoles and their activity were known.

(vi) As stated in Part III above, imidazoles are a common component of a large number of natural products, such as purine, histamine and histidine. Due to its varied high therapeutic properties, the incorporation of the imidazole nucleus was and continues to remain a common synthetic strategy during drug discovery. Amongst other therapeutic uses, imidazole derivatives had reported to possess antiviral activity. [(i) K. Shalini, et al., “Imidazole and its biological activities”, (2010) Der Chemica Sinica 1(3): 36–47 and (ii) Narasimhan, et al., “Biological importance of imidazole nucleus in the new millennium”, (2011) Medicinal Chemistry Research 20:1119–11140; published online: 6 November 2010]

(vii) More specifically, the anti-HCV activity of polycyclic compounds containing imidazole was already known. WO ’601 (Exhibit 4) discloses various polycyclic imidazole containing compounds as antivirals with HCV NS5A inhibitory activity for the treatment of HCV infection. For example, compound KC, whose structure is set out in Part VI above, was known to Exhibit anti-HCV activity with EC$_{50}$ of 0.0044 nM.

(viii) Additionally, fused ring compounds containing imidazole, including condensed imidazolylimidazoles, had also been reported to Exhibit antiviral activity for HCV infection treatment by inhibiting viral replication by inhibiting HCV NS5A protein [See for example, Exhibit 5, WO ’534]
Thus, imidazole containing compounds containing polycyclic core and those having condensed imidazolylimidazoles were known to have antiviral activity by inhibiting HCV NS5A protein.

The claimed compound is a new form of such known substances with known anti-HCV activity. The Complete Specification accompanying the present Application fails to demonstrate enhanced anti-HCV activity for *velpatasvir* (Claim 1 and Claim 4) over the known substances.

In addition and without prejudice to the above, as shown in Part VI.A above, *velpatasvir* was in the public domain and was a known substance.

Claim 1 of the present Application relates to *velpatasvir* or a pharmaceutically acceptable salt thereof. Claims 2, 3, 5 and 6 claim compositions and combinations containing *velpatasvir*. The Complete Specification accompanying the present Application does not allege an enhanced efficacy for the pharmaceutically acceptable salt thereof or the claimed pharmaceutical compositions of *velpatasvir* comprising a carrier or pharmaceutical compositions comprising an NS5B inhibitor.

The Patent Applicant has not shown significantly enhanced efficacy for the claimed compounds or the claimed compositions. Therefore, the Patent Applicant has failed to discharge the burden of showing enhanced therapeutic efficacy for Claim 1 inasmuch as it relates to a pharmaceutically acceptable salt of *velpatasvir* and Claims 2, 3, 5 and 6.
Therefore, Claim 1 to 6 fail under section 3(d) and therefore ought to be rejected under section 3(d) read with section 25(1)(f) of the Patents Act.

VI.D. SECTION 25(1)(f): FAILURE TO MEET SECTION 3(e)

(i) Section 25(1)(f) provides a ground of opposition on the ground that the subject of any claim is not an invention within the meaning of the Patents Act or is not patentable under the Patents Act.

(ii) Section 3(e) provides that 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 are not inventions within the meaning of the Patents Act.

(iii) Claims 2 and 5 claim a pharmaceutical composition comprising velpatasvir or a pharmaceutically salt thereof and a pharmaceutically acceptable carrier. Similarly, Claims 3 and 6 claim a pharmaceutical composition comprising velpatasvir or a pharmaceutically salt thereof, a pharmaceutically acceptable carrier and an NS5B polymerase inhibitor.

(iv) These claims are directed to substances obtained by mere admixture which result only in the aggregation of the properties of the components thereof.

(v) As shown above, velpatasvir was already known. The Complete Specification accompanying the present Application is silent on any synergistic effect for these claimed compositions.
(vi) The Patent Applicant has failed to show synergistic effect for the claimed compositions. As Claim 2, 3, 5 and 6 relate to a mere admixture of two or more substances that results only in the aggregation of the properties of the components thereof, it fails the test of section 3(e).

(vii) Therefore, Claims 2, 3, 5 and 6 ought to be rejected under section 3(e) read with section 25(1)(f) of the Patents Act.

VI.E. SECTION 25(1)(f): NOT A NEW INVENTION

(i) Section 25(1)(f) provides a ground of opposition on the ground that the subject of any claim is not an invention within the meaning of the Patents Act or is not patentable under the Patents Act.

(ii) It has been stated in Bayer Corporation v. Union of India AIR 2014 Bom 178 that “Patent Law is a species of intellectual property law. A right to intellectual property is an invisible/ intangible right to a product of a man's brain/ mind such as a new invented product i.e. property of the mind as against a right for material things/ tangibles i.e. goods such as a right to the invented goods. … The object of the patent law is to encourage scientific research, new technology and industrial progress. The grant of a patent necessarily means a new invention of commercial utility.”

(iii) “New”ness is an inherent requirement for an invention. If something is not new, it cannot be termed as an invention.
(iv) The term “invention” has been defined under section 2(1)(j) to mean a new product or process involving an inventive step and capable of industrial application. The definition of “inventive step” as set out in section 2(1)(ja) has been reproduced hereinabove. Section 2(1)(l) defines “new invention” as “any invention … which has not been anticipated by publication in any document … in the country or elsewhere in the world before the date of filing of the patent application with complete specification, i.e., the subject matter has not fallen in public domain or that it does not form part of the state of the art”. (emphasis supplied). It is the humble submission of the Opponent that “invention” as understood in the Patents Act would require the three definitions— invention, inventive step and new invention—to be read together, as all three describe the meaning and feature of an invention that is patentable under the law.

(v) WO 2012/068234 titled “Antiviral compounds” published on 24 May 2012 (hereinafter referred to as “WO ’234”), a copy of which is enclosed hereto as “Exhibit 8”, discloses antiviral compounds. WO ’234 was published prior to the filing date of the present Application. WO ’234 specifically discloses the claimed compound, velpatasvir, as well as the method of its synthesis [Exhibit 8, WO ’234, Example PY, pages 1100–01 and Compound 599, page 1286]. It also discloses salts of the compounds disclosed therein [Exhibit 8, WO ’234, pages 116–17], pharmaceutical formulations comprising the compounds disclosed therein with conventional carriers and excipients [Exhibit 8, WO ’234, pages 134–40] and combinations of the compounds disclosed therein
with other therapeutic agents, including NS5B polymerase inhibitors [Exhibit 8, WO ’234, pages 140–44].

(vi) Claims 1 to 6 of the present Application, being anticipated by publication before the filing date of the present Application, do not constitute a “new invention” within the meaning of section 2(1)(l) of the Act read with section 2(1)(j) and section 2(1)(ja).

(vii) As shown in Part VI.A and Part VI.B above, Claims 1 to 6 of the present Application were anticipated before the priority date and lack inventive step, do not satisfy the definition of “invention” and are not an invention within the meaning of the Act.

(viii) Therefore, the subject of Claims 1 to 6 are not an invention within the meaning of the Patents Act and ought to be rejected under section 2(1)(l), section 2(1)(j) and section 2(1)(ja) and section 25(1)(f) of the Patents Act.

40. Thus, for all the reasons stated above, the present Application ought to be rejected in its entirety.

41. As permitted under section 25(1) of the Patents Act read with Rule 55 of the Rules, the Opponent requests that the Patent Office immediately furnish the Opponent a copy of any reply and evidence, if any, filed by the Patent Applicant to this representation by way of opposition and amendment to the Complete Specification and / or claims, if any, and also permit it to file response / rejoinder to the same. The Opponent also craves leave to that it be permitted to amend the pleadings and / or grounds in its representation by way of opposition and submit further
documents and evidence, as and when necessary and especially in reply to the Patent Applicant’s reply and / or in response to any amendments that the Patent Applicant may make to the Complete Specification or claims.

42. The Opponent also requests a hearing in the present matter.

43. The Opponent also craves leave to refer to and rely upon the full text of documents, both patent and non-patent literature, referred to in the representation by way of opposition.

44. The Opponent reiterates that the fundamental right to health has paramount importance and states that a patent application that does not meet the patentability standards set out in the Indian patent law ought to be rejected.

45. The Opponent states that grant of patents to the Patent Applicant in other jurisdictions cannot be tantamount to a grant of a patent in India. The Indian patent law is different from the patent laws of other jurisdictions. Indian Parliament has deliberately set higher standards to disallow patents for pharmaceutical products that are not new, are not genuinely inventive, that are obvious to a person skilled in the art or that do not involve a technical advance. The Indian patent law also specifically prohibits grant of patents for new forms of known substances and mere admixtures of known substances. These higher standards have been set to prevent abuse of the patenting mechanism and to prevent undeserving patents from being granted.
46. The Opponent states that the present Application ought to be rejected as various publications that predate the priority date of the present Application anticipate the claims of the present Application. Novelty or “newness” is destroyed when the essential elements are disclosed in a prior art document and also when the claimed invention is inherently anticipated. The prior art document cited in Part VI.A above shows that Claims 1 to 6 of the present Application are not new, lack novelty and are anticipated by prior publication. Therefore, these claims ought to be rejected under section 2(1)(j) read with section 25(1)(b) of the Patents Act.

47. Further, the invention so far as claimed in Claims 1 to 6 is obvious to a person skilled in the art. The prior art documents cited in Part VI.B above show that Claims 1 to 6 of the present Application are obvious to a person skilled in the art. They do not involve any technical advance. The alleged invention thus lacks inventive step. Therefore, Claims 1 to 6 ought to be rejected under section 2(1)(j) and section 2(1)(ja) read with section 25(1)(e) of the Patents Act.

48. Claims 1 to 6 relate to a new form of known substances for which the Patent Applicant has not shown significant enhancement of therapeutic efficacy. Further, a part of Claim 1 and Claims 2, 3, 5 and 6 of the present Application relate to a new form of velpatasvir, a known substance, for which the Patent Applicant has not shown significant enhancement of therapeutic efficacy. The Patent Applicant has also not shown synergistic effects for Claims 2, 3, 5 and 6. As such, these claims are not patentable under section 3(d) and section 3(e) of the Patents Act. Additionally, the subject matter of Claims 1 to 6 is not a new invention within the
meaning of the Patents Act. Therefore, these claims ought to be rejected under sub-sections (d) and (e) of section 3 and clauses (j), (ja) and (l) of sub-section (1) of section 2, as the case may be, read with section 25(1)(f) of the Patents Act.

VIII. PRAYERS

49. Having established non-patentability of the impugned invention and having adduced supporting evidence for each of the above grounds of Opposition, the Opponent prays for the following reliefs:—

(a) That Patent Application bearing No. 4351/DELNP/2013 and bearing title “Condensed Imidazolylimidazoles as antiviral compounds” be rejected in toto and the grant of patent to the said Application be refused;

(b) That copy of the reply of the Patent Applicant and evidence, if any, and / or amendment to the Complete Specification or claims, if any, be forwarded forthwith to the Opponent;

(c) That the Opponent be allowed to file response / rejoinder to the reply and evidence, if any, filed by the Patent Applicant;

(d) That the Opponent be allowed to amend the pleadings and / or grounds in its representation by way of opposition and submit further documents and evidence, as and when necessary and especially in reply to the Patent Applicant’s reply and / or in response to any amendments that the Patent Applicant may make to the Complete Specification or claims;

(e) That the Opponent be granted a hearing under section 25(1) read with Rule 55;
(f) That the Opponent be granted leave to refer to and rely upon the full text of documents, both patent and non-patent literature, referred to in the representation by way of opposition;

(g) For costs;

(h) For such other and further reliefs that the Learned Controller may deem necessary in the facts and circumstances of this case.

All communications relating to these proceedings may be sent to the following address in India:—

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Dated this 1st day of November, 2017

[Signature]
Dr. GOPAKUMAR G. NAIR
Regn. No: IN/PA 509
(Agent for the Opponent)
Gopakumar Nair Associates

To,
The Controller of Patents
The Patent Office
Delhi.