March 15, 2021

Online/ Hard Copy

To,
The Controller of Patents
The Patent Office
CP 2, CP Block,
Sector V, Bidhannagar
Kolkata, West Bengal 700091
India

Re: REPRESENTATION U/S 25(1) OF THE PATENTS ACT – BY G. SRINIVASA RAO AGAINST INDIAN PATENT APPLICATION NO. 201737015848 filed on 05/05/2017
APPLICANT: VERTEX PHARMACEUTICALS INCORPORATED
Representation filed by: G. Srinivasa Rao

Respected Sir,

I/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. In this connection, we are enclosing herewith the two sets of following documents for your consideration.

1. Form 7A,
2. Index to the list of documents,
3. Written statement of Representation and
4. Documents in support of written statement.

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,

G. Sreenivasa Rao,
spiProPAT Intellectual Property Solutions.
(Opponent)

Encl: As above

C.C.: ANAND AND ANAND
B-41, NIZAMUDDIN EAST
NEW DELHI – 110013
Email.: email@anandandanand.com

BEFORE THE CONTROLER OF PATENTS, THE PATENT OFFICE, KOLKATA

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. **201737015848 filed on 05/05/2017** by **VERTEX PHARMACEUTICALS INCORPORATED**

REPRESENTATION BY:

G. SRINIVASA RAO .....OPPONENT

VS.

VERTEX PHARMACEUTICALS INCORPORATED .....APPLICANT

PRE-GRANT OPPOSITION BY G. SRINIVASA RAO

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	potential applicationto the treatment of osteoporosis" ***Bioorganic & Medicinal Chemistry Letters 16 (2006) 5659–5663***	
7.	**Annexure 5:** Copy of WO 2013/185112	842-1190
8.	Power of Attorney	

Dated this Fifteenth (15th) day of March, 2021

G. Srinivasa Rao
spiProPAT Intellectual Property Solutions
(Opponent)

To,
The Controller of Patents
The Patent Office, Kolkata

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

1.	State names, address and nationality.	I, G. Srinivasa Rao, having address at spiProPAT Intellectual Property Solutions, 2nd Floor, Above Apollo Clinic, Suresh Square, Plot No 1-58/91/SS, Survey No. 228 & 229/1, Madinaguda, Miyapur, Hyderabad, Telangana State, India– 500049 hereby give representation by way of opposition to the grant of patent in respect of Indian National Phase Application No. 201737015848 filed on 05/05/2017 made by VERTEX PHARMACEUTICALS INCORPORATED on the grounds:
2.	State the grounds, taken one after another.	on the grounds: i. Section 25(1)(e)-Obviousness/Lack of Inventive step ii. Section 25(1)(f)-Not an invention iii. Section25(1)(g)-Complete specification does not sufficiently and clearly describe the invention iv. Section 25(1)(h) - Failure to disclose information or furnishing false information relating to foreign filing
3.	Complete address including postal index number/code and state along with Telephone and fax number.	Our address for services in India is spiProPAT Intellectual Property Solutions 4th Floor, Above Apollo Clinic, Suresh Square, Plot No 1-58/91/SS, Survey No 228 & 229/1, Madinaguda, Miyapur, Hyderabad, Telangana State, India- 500049. Tel. No. 040-40240129
4.	To be signed by the opponent or by his/her authorized registered patent agent.	Dated this Fifteenth (15th) day of March, 2021.
5.	Name and designation of the natural person who has signed.	G. Srinivasa Rao, spiProPAT Intellectual Property Solutions. (Opponent)

To,
The Controller of Patents,
The Patent Office, Kolkata

THE OFFICE OF THE CONTROLLER OF PATENTS, KOLKATA

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 Application No. **201737015848 filed on 05/05/2017** by **VERTEX PHARMACEUTICALS INCORPORATED**

IN THE MATTER OF:

G. SRINIVASA RAO

.....OPPONENT

VS.

VERTEX PHARMACEUTICALS INCORPORATED .....APPLICANT

STATEMENT OF CASE OF OPPONENT

1. The Petitioner/Opponent has learnt that the Applicant has filed an ordinary application No. **201737015848** (hereinafter "the Impugned Application") on05/05/2017. The Impugned application was published in the Official Journal of the patent office on 25/08/2017.

2. The Impugned application is entitled “MODULATORS OF CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR”. The impugned application was filed with 185 claims.

3. The opponent by way of present pre-grant opposition submits that the claims currently pending on record are not patentable under the provisions provided in this Act. Theclaims currently on record are annexed herewith as **Annexure-1**.

GROUNDS OF OPPOSITION

4. The Opponent submits its opposition by way of representation under Section 25(1) in respect of the said Indian Patent Application No. **201737015848** on the following grounds below, which are without prejudice and in the alternative to each other.

   i) **Section 25(1)(e)-Obviousness/Lack of Inventive step**
   ii) **Section 25(1)(f)-Not an invention**
   iii) **Section 25(1)(g)-Complete specification does not sufficiently and clearly describe the invention**
   iv) **Section 25(1)(h) - Failure to disclose information or furnishing false information relating to foreign filing**

GROUND I

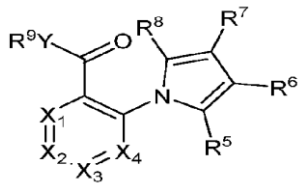
5. **Section 25(1)(e): Lack of inventive step**-*The invention so far as claimed in any claim of the complete specification is obvious and clearly does not involve any inventive step, having regard to the matter published as mentioned in clause (b) or having regard to what was used in India before the priority date of the claim.*

6. The technical teaching of the impugned invention applies to limited knowledge which is well known in art without any inventiveness. It is submitted that the claims are obvious and lack any inventive step in view of teachings, motivation and suggestion in various prior art documents listed herein below.

7. It is submitted that the impugned application is obvious in light of teachings of following prior art documents:

    - WO 2014/071247 Al (annexed herewith as **Annexure 2)**
    - WO 2009/032116 (Annexed herewith as **Annexure 3)**
    - Corey R. Hopkins et al Design and synthesis of novel N-sulfonyl-2-indole carboxamidesas potent PPAR-c binding agents with potential applicationto the treatment of osteoporosis"***Bioorganic & Medicinal Chemistry Letters 16 (2006) 5659–5663;*** **published in 2006** (Annexed herewith as **Annexure 4**)
    - WO 2013/185112 (**Annexure 5**)

8. The prior art document **WO 2014/071247**, hereinafter referred to as WO'247, published on 08 May 2014 discloses a compound of formula I-A



I-A

Where;
Xi is CR or N;
X2 is CR2 or N;
X3 is CR3 or N;
X4 is CR4 or N;
wherein no more than three of Xi, X2, X3, and X4 are N;
Y is -O- or -S(=0) 2-N(R N)-;

R1, R2, R3, and R4 are independently selected from the group consisting of -L-Z,hydrogen, halo, -CN, -NO2, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heteroaryl, -ORA, -N(RB)2, -SRA, -C(=0)R A, -C(=0)OR A, -C(=0)SR

A, -C(=0)N(R B)2, -OC(=0)R A, -NRBC(=0)R A, -NRBC(=0)N(R B)2, -SC(=0)R A, -C(=NRB)RA, -C(=NRB)N(RB)2, -NRBC(=NRB)RB, -C(=S)RA, -C(=S)N(RB)2, -NRBC(=S)RA, -S(=0)R A, -S0 2RA, -NRBS0 2RA, and -S0 2N(RB)2;

each RA is independently hydrogen, optionally substituted alkyl, optionallysubstituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl,optionally substituted heterocyclyl, optionally substituted aryl, or optionally substitutedheteroaryl;

each R is independently hydrogen, optionally substituted alkyl, optionally substitutedalkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionallysubstituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or twoRB groups are taken together with their intervening atoms to form an optionally substitutedheterocyclic ring;

R5, R6, R7, and R8 are independently selected from the group consisting of -L-Z,hydrogen, halo, -CN, -NO 2, optionally substituted alkyl, optionally substituted alkenyl,optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted aryl,optionally substituted heterocyclyl, optionally substituted heteroaryl, -ORA, -N(RB)2, -SRA, -C(=0)R A, -C(=0)OR A, -C(=0)SR A, -C(=0)N(R B)2, -OC(=0)R A, -NRBC(=0)R A, -NRBC(=0)N(R B)2, -SC(=0)R A, -C(=NRB)RA, -C(=NRB)N(RB)2, -NRBC(=NRB)RB, -C(=S)RA, -C(=S)N(R B)2, -NRBC(=S)RA, -S(=0)R A, -S0 2RA, -NRBS0 2RA, and -S0 2N(RB)2;

or R5 and R6 are taken together with their intervening atoms to form an optionally substituted, fused, partially unsaturated or aromatic ring having 0-3 heteroatoms independently selectedfrom nitrogen, oxygen, and sulfur; or R6 and R7 are taken together with their interveningatoms to form an optionally substituted, fused, partially unsaturated or aromatic ring having0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or R7 and R8 aretaken together with their intervening atoms to form an

optionally substituted, fused, partiallyunsaturated or aromatic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

R9 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionallysubstituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl,optionally substituted aryl, optionally substituted heteroaryl, or an oxygen protecting group when attached to an oxygen atom; RN is hydrogen, optionally substituted alkyl, or a nitrogen protecting group;

each L is independently a bond, -0-, -S-, -N(R)-, -C(O)-, -C(0)N(R)-, -N(R)C(0)N(R)-, -N(R)C(0)-, -N(R)C(0)0- -OC(0)N(R)-, -S0 2- -S0 2N(R)-, -N(R)S0 2- -OC(O)-, -C(0)0- -C(0)N(R)N=C(R')-, an optionally substituted membered cycloalkylene, an optionally substituted 4-7 membered heterocyclylene, anoptionally substituted 5-6 membered heteroarylene, an optionally substituted phenylene, or anoptionally substituted, straight or branched, Ci-6 alkylene, C2 -6 alkenylene, or C2 -6 alkynylenechain, wherein one, two, or three methylene units of L are optionally and independentlyreplaced by -0-, -S-, -N(R)-, -C(O)-, -C(0)N(R)-, -N(R)C(0)N(R)-, -N(R)C(0)-, -N(R)C(0)0- -OC(0)N(R)-, -S0 2- -S0 2N(R)-, -N(R)S0 2- -OC(O)-, -C(0)0- -C(0)N(R)N=C(R')- an optionally substituted 3-7 membered cycloalkylene, an optionallysubstituted 4-7 membered heterocyclylene, an optionally substituted 5-6 memberedheteroarylene, or an optionally substituted phenylene;

each R is independently hydrogen, optionally substituted Ci_6 alkyl, optionallysubstituted C2-6 alkenyl, or optionally substituted C2-6 alkynyl, or R and an optionalsubstituent on Cy are taken together with their intervening atoms to form a 5-6 memberedheterocyclic fused ring;each R' is independently hydrogen, optionally substituted alkyl, optionally substitutedalkenyl, optionally substituted alkynyl, or an optionally substituted, monocyclic or bicyclic,saturated, partially unsaturated, or aromatic ring having 0-4 heteroatoms independentlyselected from nitrogen, oxygen, and sulfur, or R' and an optional substituent on Cy are takentogether with their

intervening atoms to form a 5-6 membered carbocyclic or heterocyclicfused ring;

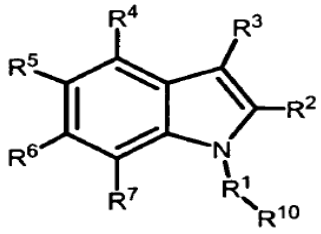
each Z is independently optionally substituted alkyl, optionally substituted alkenyl,optionally substituted alkynyl, or Cy; and

each Cy is independently an optionally substituted, monocyclic or bicyclic, saturated,partially unsaturated, or aromatic ring having 0-4 heteroatoms independently selected fromnitrogen, oxygen, and sulfur;

When the substituents disclosed in WO'247 are applied to formula Ia, the document discloses three compounds similar to the claimed compound 1 of the impugned application.

9. It is evident from the disclosure of the above prior art that the three-ring system and the substitutionswerewell before the filing of the impugned application.

10. WO 2009/032116 published on 12th March 2009hereinafter referred to as WO'116 discloses compound of formula 1;

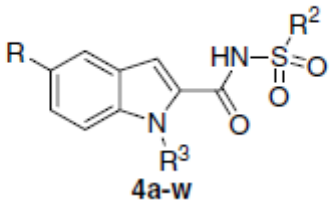


(I)

11. The WO'116 covers and disclose number of compounds like compound number 18, 57, 59, 63, 77, 105, 118, 120, 121-124, 134-135, 137, 142,151,153,154,163,168,171-175,188,190,195,
198,213,217,220,221,224,231,232,235,236,240,241,245,246,251,252,254-256,262-264,266-269,271,274,275,277,278,290
295,303,306,308,317,319,320,323,324-330,332-334,
336,339,341,342,344-345,347,348,351-353,355-357,360,361,363,366-371,375,377-379,380-383,385,386,388,391,393-401,405-415,418,419,421-430,432,434,436-454,461,462,464-466,469,471-

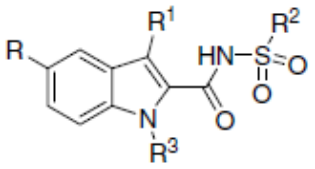
491,493,494,495,497,498,500-503, 505-601, 604-605, 614, 617, 620-630.

12. Corey R. Hopkins et al discloses synthesis of novel N-sulfonyl-2-indole carboxamides.The document further discloses;



4a-w

Compound	R	R^2	R^3
4a	H	Ph	3-CF_3Bn
4b	H	4-F–Ph	3-CF_3Bn
4c	H	4-Cl–Ph	3-CF_3Bn
4d	H	3-CF_3–Ph	3-CF_3Bn
4e	H	4-CH_3Ph	3-CF_3Bn
4f	H	2-CH_3Ph	3-CF_3Bn
4g	H	2-Naphthyl	3-CF_3Bn
4h	H	2-CF_3–Ph	3-CF_3Bn
4i	H	2-(5-Chlorothiophene)	3-CF_3Bn
4j	H	Me	3-CF_3Bn
4k	H	4-CF_3–Ph	4-CF_3Bn



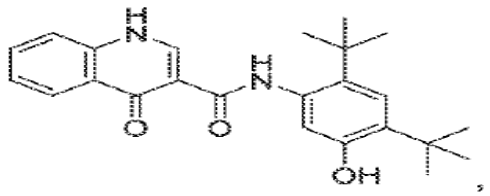
2a-f

Compound	R	R^1	R^2	R^3
2a	H	4-CH_3OPh	Ph	3-CF_3Bn
2b	H	4-CH_3OPh	4-F–Ph	3-CF_3Bn
2c	H	4-CH_3OPh	3-CF_3–Ph	3-CF_3Bn
2d	H	4-CH_3OPh	2-CO_2MePh	3-CF_3Bn
2e	H	4-CH_3OPh	2-CH_3Ph	3-CF_3Bn
2f	H	4-CH_3OPh	Me	3-CF_3Bn

13. It is a well-known fact in pharmaceutical drug development that Pyridine moieties are often used in drugs because of their characteristics such as basicity, water solubility, stability, and hydrogen bond-forming ability, and their small molecular size. Further pyridine rings are able to act as the bio isosteres of amines, amides, heterocyclic rings containing nitrogen atoms, and benzene rings, their replacement by pyridine moieties is important in drug discovery.

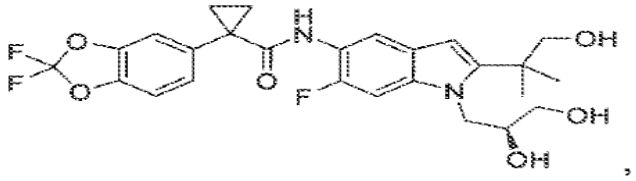
14. The teachings of Corey R. Hopkins et and WO'116 in light of the common general knowledge regarding the isosteric replacements renders the compounds as disclosed in the claimed invention obvious to a person skilled in the art.

15. WO 2013/185112 published on 12th December 2013 hereinafter referred to as WO'112 discloses pharmaceutical compositions for the treatment of cftr - mediated disorders.WO'112 discloses a compound composition of formula I and pharmaceutically acceptable salts for treating a CFTR-mediated disease.



Compound 1

16. The WO'112 document further discloses a compound of formula 3 for the same purpose;



17. The document also teaches method of treating a CFTR-mediated disease in a patient comprising administering Compound 1, or

pharmaceutically acceptable salt thereof, in combination with Compound 3 in a patient comprising administering Compound 1 .

18. The disclosure of the above WO document renders claims 21-24 obvious and devoid of any inventive steps.

19. Hence, in view of the disclosure of aforesaid prior art documents the invention claimed in the impugned application lacks inventive step.

GROUND II

Section 25(1) (f)-Not an invention

Claims of impugned application are not patentable as per Section 3(d)

20. Section 3(d) states "the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.

21. As elaborated in preceding paragraphs under the Grounds of Lack of Inventive Step, the composition claimed in impugned application was known in the field before the priority date of the impugned application. Further, the specification as filed does not state any data establishing enhancement in efficacy of the claimed composition known in art, such as disclosed in the prior art documents cited hereinabove.

22. Hence, the claimed invention is not patentable as per Section 3(d) of the Act.

Claims of the impugned applicationare not patentable as per Section 3(e)

23. The Opponent states that the claimed invention clearly falls under the bar of Section 3(e) which clearly states that a product obtainedby mereadmixing resulting only in the aggregation of the properties of the components thereof or a process for producing such substance is not considered as an invention.

24. The opponent submits that the subject matter of Claims 21 to 24 of the impugned patent falls under 3(e). The applicant has merely used common general knowledge in the art and combined actives with excipients to achieve thedesired resultant composition. However, the Patentee has not disclosed any evidence or experimental data in the impugned patent outlining that the claimed dispersion displays any effect which unexpectedly supersedes the effect produced by the individual components.

25. Further the claimed composition in claim 21-24 is not defined in terms of ratio and concentration of the components which constitute the impugned patent and thus a mere admixture. The applicant has merely used common general knowledge in the art and combined actives with excipients to achieve the desired resultant composition.

26. In absence of any comparative data in the specification of the impugned application highlighting the synergistic effect of the claimed composition of the impugned patent over its individual components, the impugned patent should be rejected under section 3(e) read with section 25(2)(f) of the Act.

27. Thus, impugnedapplication is liable to be rejected on this ground alone.

GROUND III

Section 25(1)(g): Complete specification does not sufficiently describe the invention.

28. The opponent states that the complete specification of the alleged invention does not sufficiently and clearly describe the invention or the best method by which it is to be performed.

29. Thus, the disclosure of specification is not in proportion with the breadth of the claim. The Opponent further submits that the instant invention is not an invention u/s 2(1)(j) within the meaning of this act as the Patentee fails to disclose industrial applicability of the instant invention. The compounds of the instant invention are MODULATORS OF CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR. However, the Patentee fails to disclose the IC50 values of the compounds claimed in the patent.

30. Therefore, the specification of the impugned application fails to sufficiently describe the invention and the impugned application should be rejected on this basis alone.

GROUND IV

Section 25 (1) (h): The Applicant has failed to disclose to the Controllerthe information required under Section 8.

31. The applicant has not filed any Form 3 disclosing details and status of aforementioned corresponding foreign applications at the Patent Office within prescribed time. The applicant has failed to inform the Indian patent office of the same and therefore, on this ground alone the patent application should be rejected.

32. The opponents crave leave to file further submissions and evidence with respect to this ground.

P R A Y E R

In the fact and circumstances of the case, the Opponent prays as follows:

that the Indian Patent Application No. **201737015848** by VERTEX PHARMACEUTICALS INCORPORATED

i. be rejected under Section 25(1) of the Patents (Amendment) Act, 2005;
ii. the Opponent may be allowed to file further documents as evidence if necessary, to support its averments;
iii. the Opponent may be granted an opportunity of being heard in the matter before any final orders are passed;
iv. the Opponent may be allowed to make further submissions in case the applicant makes any amendments in the claims;
v. Any other reliefs considering the facts and circumstances may be granted in favour of the Opponent in the interest of justice.

Dated this Fifteenth (15th) day of March, 2021

G. Srinivasa Rao
spiProPAT Intellectual Property Solutions
(Opponent)

To,
The Controller of Patents
The Patent Office, Kolkata