$~

* **IN THE HIGH COURT OF DELHI AT NEW DELHI**

Reserved on: 6th October, 2023.
Date of decision: 9th February, 2024

\+ **C.A.(COMM.IPD-PAT) 28/2023**

OVID THERAPEUTICS, INC. ..... Appellant

Through: Mr. Daksh Oberoi, Mr Kshitij Saxena & Mr. Saaransh Vijayvargiya, Advocates.

versus

ASSISTANT CONTROLLER OF PATENTS AND DESIGNS ..... Respondent

Through: Mr. Harish Vaidyanathan Shankar, CGSC, with Mr. Srish Kumar Mishra, Mr. Sagar Mehlawat, Mr. Alexander Mathai Paikaday, Mr. M Sriram and Mr. Krishnan V., Ads. (M: 9810788606)

CORAM:
JUSTICE PRATHIBA M. SINGH

JUDGMENT

PRATHIBA M. SINGH, J.

Brief Facts

1. This is an appeal under Section 117A of the Patents Act, 1970 *(hereinafter 'the Act')* challenging order dated 31st August, 2021, issued by the ld. Assistant Controller of Patents and Designs *(hereinafter 'Controller')*. By the impugned order, the Appellant's patent application bearing number 201717000025 titled *'Methods of Increasing Tonic Inhibition and Treating Secondary Insomnia' (hereinafter 'subject patent')* has been refused under Section 15 of the Act. The Bibliographic details of

the subject patent application are set out below:

APPLICATION NUMBER	201717000025
APPLICATION TYPE	PCT NATIONAL PHASE APPLICATION
DATE OF FILING	02/01/2017
APPLICANT NAME	OVID THERAPEUTICS INC.
TITLE OF INVENTION	METHODS OF INCREASING TONIC INHIBITION AND TREATING SECONDARY INSOMNIA
FIELD OF INVENTION	PHARMACEUTICALS
ADDITIONAL-EMAIL (As Per Record)	knk@kankrishme.com
PCT INTERNATIONAL APPLICATION NUMBER	PCT/US2015/034018
PCT INTERNATIONAL FILING DATE	03/06/2015
PRIORITY DATE	06/06/2014
REQUEST FOR EXAMINATION DATE	18/05/2018
PUBLICATION DATE (U/S 11A)	07/04/2017
REPLY TO FER DATE	13/02/2020

2. The Appellant filed the present application as a National Phase Application, before the Indian Patent Office on 2nd January, 2017. The said application arose out of the PCT application dated 3rd June 2015, bearing number PCT/US2015/034018. The said application claimed priority from a US Patent Application, with a priority date of 6th June, 2014.

3. The Appellant filed the request for examination of the subject patent application on 18th May, 2018. In response to the request for examination, a First Examination Report (FER) with a statement of objections was issued

on 16th August, 2019 by the Controller. The objections raised were of lack of novelty, lack of inventive step and non- patentability under Section 3 (i) and Section 3 (e) of the Act. As per the FER, Claims 1-28 of the subject patent application were directed towards a method of treatment and fell within the scope of non-patentability under Section 3(i) of the Act. Further, it was stated that the claimed composition as per Claims 1, 4-8 and 18-28 were obtained by a mere admixture resulting only in an aggregation of the properties of the components without any synergistic effect, thereby attracting the objection under Section 3(e) of the Act. In addition, the ground of insufficiency of disclosure and definitiveness in the Claims, in violation of the requirements under Sections 10(4)(c) & 10(5) of the Act, were also raised by the Controller in the FER.

4. To substantiate the objection of lack of novelty the Controller relied on the prior art document being D1 which discloses the effect of Gaboxadol in a model of Angelman syndrome, anticipating Claims 1-28 of the subject patent application. For the purpose of lack of inventive step, prior arts D2-D5 were cited by the Controller. The details of the said prior art documents cited by the Controller are as under:

(i) D1-*Decreased Tonic Inhibition in Cerebellar Granule Cells Causes Motor Dysfunction in a Mouse Model of Angelman Syndrome* by K. Egawa et. al. with publication date 5th December, 2012;

(ii) D2- JP2012501301 A, titled *'Pharmaceutical composition comprising gaboxadol and PAT1 inhibitor or OAT inhibitor'*, with publication date 19th January, 2012;

(iii) D3-US2005/0137222 A1, titled *'Treatment of Insomnia in Humans'* with publication date 23rd June, 2005;

(iv) D4-WO2009/056146, titled *'Pharmaceutical Composition Comprising Gaboxadol and an Inhibitor of PATL or Oat'* with publication date 7th May, 2009;

(v) D5- US2011/0046090 A1 titled *'Modulation of Neurogenesis with Gaba Agents and Gaba Analogs'* with publication date 24th February, 2011.

5. A response dated 13th February, 2020 was filed to the said FER by which the Appellant amended the Claims of the subject patent to Claims 1-20, and limited the present invention to '*a composition*'. It is the stand of the Appellant that by the said amendments the Appellant had clarified the composition to be having 0.05 mg to about 30 mg of gaboxadol or a pharmaceutically acceptable salt with the said composition.

6. As per the Appellant, prior art D1 suggests only about administering low doses of 4,5,6,7-tetrahydroisothiazio-[5,4-c]pyridine-3-01(THIP) whereas the subject patent application suggests increasing tonic inhibition which will be a useful strategy for alleviation of motor dysfunction in Angelman syndrome. It was further submitted that the present composition comprises of GABA agent or GABA analog in combination with one or more neurogenic agents which is different than D5. It has further been stated that the dosage of Gaboxadol as claimed in the subject invention has not been disclosed in any of the prior art documents *i.e.* D1 to D5.

7. After perusing the response to the FER of the Appellant, the Controller gave a hearing notice dated 7th August, 2020 for the hearing scheduled on 2nd November, 2020. The Appellant attended the hearing and

thereafter submitted written submissions dated 16th September, 2020 in support of the arguments made in the hearing.

8. In the said written submissions, the Appellant submitted that daily dosing and extended improvement was not disclosed in the prior arts and could not have been predicted based on the known properties of Gaboxadol. The Appellant also deleted Claims 7, 8 and 11-20 of the amended set of Claims. Further, the Appellant has relied on STARS Phase 2 clinical trial topline data which as per the Appellant confirmed the effect of once daily administration. Dealing with the grounds of lack of novelty and lack of inventive step, the Appellant relied on the declaration by the inventor of the subject patent application *i.e.*, Matthew During to prove synergistic effect of the ingredients of the Claim 1. In respect of the grounds of insufficiency of disclosure under Section 10(4) of the Act, the Appellant submitted that the amended set of Claims have been given and Claim 11 has been deleted.

9. The ld. Controller after considering the submissions of the Appellant, refused the subject patent application under Section 15 of Act on the following grounds:

(i) non-patentability under Section 3(d), Section 3(e);

(ii) lack of inventive step over the cited prior art documents as required under Section 2(1)(ja);

(iii) insufficiency of disclosure, in violation of the requirements in Section 10(4), Section 10(5) and;

(iv) broadening the scope of the Claims in violation of Section 59 of the Patent Act, 1970.

10. Aggrieved with the said decision of the ld. Controller, the Appellant has filed the present Appeal under Section 117A of the Act.

Submissions

11. Ld. Counsel for the Appellant made the following submissions during the course of hearing of the Appeal:

(i) that since the subject patent application came through the PCT route, the Appellant could not change the originally filed Claims before filing the National Phase Application;

(ii) that the pharmaceutical composition as claimed was also contained in the main Claim of the originally filed Claims;

(iii) that the prior art document D1 discloses that high doses of Gaboxadol may cause adverse effects, so explicitly it proposes that low doses of Gaboxadol potentially may be an effective treatment for the Cerebellar Ataxia in Angelman syndrome. Therefore, administration of about 10 mg to about 50 mg Gaboxadol for the treatment of Angelman Syndrome would not have been considered obvious to one skilled in the art based on the disclosure in D1;

(iv) that a single daily dose would not be expected to provide long term improvements and thus the present invention involves an inventive step;

(v) that the STARS Phase 2 clinical trial topline data confirms the effect of once daily administration.

12. Further, in respect of the objection raised under Section 59 of the Act, it was argued that the Claims are clear and succinct based on the subject matter disclosed in the specification and pharmaceutical composition.

13. *Per Contra*, Mr. Harish V. Shankar, ld. CGSC submits that the

composition consisting of 4,5,6,7-tetrahydroisothiazio-[5,4-c]pyridine-3-01 (THIP) is a known pharmaceutical composition. It is only the dosage that was sought to be changed by the Appellant and thus the application has been rightly rejected by the Controller.

Analysis & Conclusions

14. The PCT application bearing number 201717000025 titled *'Methods of increasing tonic inhibition and treating secondary insomnia'* was filed with the international filing date of 3rd June, 2015 claiming priority from a US patent application dated 6th June, 2014 was filed by the Appellant. The said application entered the national phase in India on 2nd June, 2017.

15. The national phase of the PCT application had 28 claims. The said claims have been attached as **Annexure 1**, amongst which, the independent claim *i.e.*, claim 1 has been set out below:

> *"1. A method of increasing tonic inhibition of neurons in a subject comprising administering to a human subject with a neurodegenerative disease, a neurogenetic disorder, or a central nervous system disorder a pharmaceutical composition comprising an effective amount of 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase tonic inhibition of neurons of the subject. "*

16. The complete specification in the national phase application acknowledges that the field of the invention is a method of using the said composition or a derivative thereof, and the same reads as under:

> *"**FIELD OF THE INVENTION***
>
> *The field of the invention generally relates to methods of using a composition including 4,5,6,7-tetrahydroisoxazolo (5,4-c) pyridin-3-ol (THIP) a*

derivative thereof or a pharmaceutically acceptable salt thereof for treating diseases and disorders characterized by secondary insomnia and/or defects or deficiencies in tonic inhibition"

17. The summary of the invention also specifies that the subject patent application pertains to a pharmaceutical composition designed to increase tonic inhibition of neurons, with a focus on treating various medical conditions, in particular Fragile X syndrome and Angelman syndrome. Therefore, the summary indicates that the specific solution proposed in the subject patent application is founded on the introduction of a specified pharmaceutical composition and addresses the therapeutic gap in the treatment of neurological disorders. The relevant extract of the '*SUMMARY OF THE INVENTION*' is set out below:

*"**SUMMARY OF THE INVENTION***

Methods of increasing tonic inhibition of neurons in a subject, particularly subjects with Fragile X syndrome or Angelman syndrome are provided. Methods of treating secondary insomnia in a subject with a neurodegenerative disease or a central nervous system disorder are also provided. ***The methods typically include administering to the subject a pharmaceutical composition including an effective amount of 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP)*** *or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase tonic inhibition of neurons in the subject, to increase slow wave sleep (SWS) and/or slow wave activity (SWA), normalize sleep architecture, reduce secondary insomnia, increase non-rapid eye movement (REM) sleep, increase sleep continuity, enhance delta activity within NREM, increase or improve total sleep time (TST), increase or improve sleep efficiency, reduce total time*

awake (TAA), reduce number of awakenings (NWA), reduce latency to persistent sleep (LPS), or reduce wake after sleep onset (WASO) in the subject, or any combination thereof in the subject."

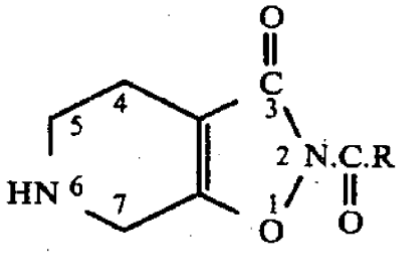
18. In the detailed description of the invention in the subject patent application, it has also been acknowledged that THIP and Gaboxadol are known in the art. The relevant paragraph of the specification reads as under:

*"**A. 4,5,6,7-tetrahydroisoxazolo (5,4-e)pyridin-3-al (THIP)***

*The compositions for use in the disclosed methods of treating secondary insomnia include 4,5,6,7-tetrahydrosoxazolol 5.4-e)pyridin-3-ol (also referred to as THIP and gaboxadol), a derivative thereof, or pharmaceutically acceptable salt thereof, or a structurally related compound THIP, as well as derivatives and structurally related compounds, and methods of making thereof **are known in the art**. See, for example, U.S. Patent Nos. 4,278,676, 4,362,731, 4,353,910, and WO 2005094820 each of which is specifically incorporated by reference herein in its entirety.*

xxx xxx xxx

***Derivatives of THIP are known in the art.** See, for examples, U.S. Patent No. 4,353,910.*



III

wherein R is an alkyl group, branched or unbranched, having from one to seventeen carbon atoms inclusive, a phenyl group optionally substituted with one or two groups selected from lower alkyl, lower alkyloxy and

halogen, a phenylalkyl group, lower alkyloxy group or a— NHR_1 group, wherein R_1 is hydrogen, lower alkyl, phenyl or cyclohexyl, as well as pharmaceutically acceptable acid addition salts thereof.

Preferred derivatives have the formula"

19. Thus, the complete specification itself acknowledges that THIP and gaboxadol were known prior to the filing of the present patent application. When read in this context, the originally filed Claim 1 of the application specifically deals with a method of increasing the tonic inhibition of neurons, when administered on a human subject with a neurodegenerative disease, with a THIP or a derivative composition. Thus, Claim 1 of application though worded as a method claim is a composition claim for THIP as a derivative thereof, specifically in respect of neurodegenerative diseases. The original 28 Claims contained in the PCT filing are now restricted to 8 Claims, and all the limitations in the original Claims are now sought to be removed. The finally Amended Claims are now as under:

"1. A pharmaceutical composition comprising 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP or gaboxadol) or a pharmaceutically acceptable salt thereof wherein the composition comprises 0.05 mg to 30 mg gaboxadol or a pharmaceutically acceptable salt thereof.

2. The pharmaceutical composition as claimed in claim 1, comprising 10 mg to 30 mg gaboxadol or a pharmaceutically acceptable salt thereof.

3. The pharmaceutical composition as claimed in claim 1, comprising 5 mg to 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

4. The pharmaceutical composition as claimed in claim 1, comprising 10 mg to 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.

5. The pharmaceutical composition as claimed in claim 1, comprising 10 mg gaboxadol or a pharmaceutically acceptable salt thereof.
6. The pharmaceutical composition as claimed in claim 1, comprising 15 mg gaboxadol or a pharmaceutically acceptable salt thereof.
7. The pharmaceutical composition as claimed in claim 1, wherein the composition provides a sustained pharmacological effect for 8 hours.
8. The pharmaceutical composition as claimed in claim 1, wherein the composition provides a sustained pharmacological effect for 12 hours."

20. The impugned order dated 31st August, 2021 after considering the submissions of the Appellant, gives the following analysis:

Qua Section 59 of the Patents Act, 1970

".....
Analysis:- The object of the present invention is relates to a method of increasing tonic inhibition of neurons in a subject comprising administering to a human subject with a neurodegenerative disease, a neurogenetic disorder, or a central nervous system disorder a pharmaceutical composition comprising an effective amount of 4,5,6,7- tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase tonic inhibition of neurons of the subject. Further Applicant's agent filed the claims at the time of filing the application in National phase (as well as in at WIPO) pertains to "a method of increasing tonic inhibition of neurons in a subject comprising administering to a human subject with a neurodegenerative disease, a neurogenetic disorder, or a central nervous system disorder a pharmaceutical composition comprising an effective amount of gaboxadol or 4,5,6,7- tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) or a derivative thereof and a

pharmaceutically acceptable carrier or excipient" and in the dependant claims mainly discussing about the treating disease, treatment parameters, mode of administration and dosage of active drug. Nowhere in the claims discuss about the gaboxadol composition or components of the composition. Applicant agent filed the amended set of claims 1-20 to FER reply and also filed claims 1-8 to hearing reply but those amended claims 1-8 does not fall within the scope of the invention as originally filed claims as well as not supported the specification. Hence the amended claims 1-8 are not allowable under section 59 of the Patents Act, 1970."

Qua Section 10(5) and 10(4) of the Patents Act, 1970

"…….

Analysis:-The applicant agent filed the amended set claims 1-8, which are not supported by the description. Further the subject matter of the present invention relates to a method of increasing tonic inhibition of neurons but the amended claims 1-8 relates to gaboxadol composition. Furthermore, the amended claims claiming that composition but there is only one active component disclosed that means it cannot be considered as composition and also no specific support for the composition disclosed in the specification. Therefore the amended set of claims 1-8 are not supported under section 10(5) and 10(4) of the Indian Patents Act, 1970."

Qua Section 2 (1) (ja) of the Patents Act, 1970

"…….

Analysis:- The applicant agent filed the amended claims 1-8, which are not inventive over the cited Prior art document D1-D5 since the subject matter of the claims 1-8 of the present invention relates to to gaboxadol composition but the components present in the composition only one component that is gaboxadol.

That mean it should be considered as compound not the composition. The compound present in the present invention is already known in the cited documents D1-D5. Therefore the claims 1-8 of the present invention are not inventive over cited documents D1-D5 under section 2(1)(ja) of the Indian Patents Act, 1970."

Qua Section 3 of the Patents Act, 1970 for Non- Patentability

"…..

Analysis:- Claims 1-8 fall within the scope of such clause (d) of section 3 of Patents Act, 1970-The compounds as defined in the claims are not novel and inventive. In view of the compounds as mentioned in the prior art(see above), the compounds of the present invention would be considered as "same compounds" as per the clause/Act.

b) Claims 1-8 is fall within the scope of such clause (e) of section 3 of Patents Act, 1970-no composition or dosage has been disclosed.

Hence, the amended claims 1-8 are not allowable u/s 3(d) and 3(e)of the patents Act, 1970."

21. To summarise, the rejection by the Controller is based on the following grounds:

a) that the amended claims are not supported by the description as the initial Claims were method Claims but the final Claims are composition Claims. The amended Claims 1-8 do not fall within the scope of the originally filed Claims. The composition Claims do not find any support in the complete specification.

b) The amended Claims are not inventive as prior art documents D-1 to D-5 relate to the various Gaboxadol compositions which are already known.

c) The Claims are affected by both Section 3(d) and Section 3(e) of the Act, since the composition has not been disclosed and merely a reference to the compound already documented in prior arts has been made.

22. Having considered the originally filed claims, the amended claims and the impugned order, the main question that arises is:

Whether the amended Claims are within the scope of original Claims?

23. Claim 1 is the only independent Claim in both the amended claims as also the original claims. A comparative analysis of original Claim 1 and amended Claim 1 is as follows:

Original Claim No. 1 ***Originally filed on 2nd January, 2017***	**Amended Claim No.1** ***Filed on 16th September, 2020***
A method of increasing tonic inhibition of neurons in a subject comprising administering to a human subject with a neurodegenerative disease, a neurogenetic disorder, or a central nervous system disorder a pharmaceutical composition ***comprising*** *an effective amount of 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase tonic inhibition of neurons of the subject.*	*A pharmaceutical composition comprising 4,5,6,7tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP or gaboxadol) or a pharmaceutically acceptable salt thereof wherein the composition comprises 0.05 mg to 30 mg gaboxadol or a pharmaceutically acceptable salt thereof.*

24. There are three differences between the originally filed Claim 1 and the amended Claim 1. The same are as under:

(i) that the amended Claim omits the limitation and also reference

to the specific disease for which the composition is intended;

(ii) that the amended Claim pertains to a composition Claim, while the initially filed Claim relates to a method as also a composition Claim;

(iii) that the amended Claim specifies the range of Gaboxadol that is to be used.

25. As noted above, although the originally filed Claim 1 is worded as a method claim, it is in fact a composition claim. Insofar as the difference in (i) above, is concerned, the limitations which existed in claim 1 do not exist in the amended claim. Thus, in respect of the first difference that has been observed, the amended claim 1 has not mentioned the disease for which the said composition has been used - to that extent it can be argued that the claim is sought to be broadened in the amendment. The limitation as contained in original claim 1 *i.e.*, limiting the claims to a neuro degenerative disease, a neurogenetic disorder or a central nervous system disorder is absent and thus the objection under Section 59 of the Act is valid. Insofar as the difference in (ii) and (iii) above is concerned, since the amended Claim specifies the range of gaboxadol that is to be used, it can be said that the amended claims restrict the scope of the invention and makes it narrower. Section 59 of the Act deals with the scope of amendment, which reads as under:

> *"59. Supplementary provisions as to amendment of application or specification.—*
> *(1**) No amendment of an application for a patent** or a complete specification or any document relating thereto shall be made except by way of disclaimer, correction or explanation, and no amendment thereof shall be allowed, except for the purpose of*

> *incorporation of actual fact, and no amendment of a complete specification shall be allowed, the effect of which would be that the specification as amended would claim or describe matter not in substance disclosed or shown in the specification before the amendment, or that any claim of the specification as amended would not fall wholly within the scope of a claim of the specification before the amendment*
> *(2) Where after the date of grant of patent any amendment of the specification or any other documents related thereto is allowed by the Controller or by the High Court, as the case may be,—*
> *(a) the amendment shall for all purposes be deemed to form part of the specification along with other documents related thereto;*
> *(b) the fact that the specification or any other documents related thereto has been amended shall be published as expeditiously as possible; and*
> *(c) the right of the applicant or patentee to make amendment shall not be called in question except on the ground of fraud.*
> *(3) In construing the specification as amended, reference may be made to the specification as originally accepted."*

26. A bare reading of the above stated Section 59(1) of the Act shows that the amended Claim has to be within the amended scope of unamended Claims and within the complete specification. In this instance, the omission of the name of the disease in the amended claim expands the scope within which the composition can be applied and therefore, the amended Claim 1 expands the scope of the subject patent.

27. Further in ***Sulphur Mills Ltd. v. Dharamaj Corp Guard Ltd. & Anr., 2021:DHC:2262*** it has been observed that the modification and variation can be done as long as they are within the scope of original filed claims. The

relevant portion of the same reads as under:

> *The view having been that the amendments are in accordance with Section 59 of the Patents Act, 1970, the mere fact that the Plaintiff has amended the claims would not weigh against the Plaintiff. It is usual for patent applicants to edit, amend, modify and vary the claims during the examination and opposition process. So long as the amendments sought are within the scope of the claims originally filed, no adverse conclusion can be drawn on the basis of the said amendments.*

28. In the present case the field of description clearly describes that this method and composition is to be used for the purpose of treating secondary insomnia and the fact that the medical condition is not written in the amended claims show that the same has gone beyond the specification as also the description of the invention.

29. In respect to the third difference as stated above, it is seen that they have specified the amount of gaboxadol that is to be used which is clarifying an earlier claimed feature. It has been observed in ***Nippon A&L Inc. v. The Controller of Patents, 2022:DHC:2434*** that so long as the amended Claim is clarificatory in nature or disclaims earlier claimed feature, they can be allowed. The relevant portion of the judgement is as under:

> *"53. The import of these paragraphs of the Ayyangar Committee Report has been considered by the IPAB in Tony Mon George (supra) and it has held that the Report favours wider scope of amendment before acceptance to that after acceptance. The IPAB concluded that if the amended claims define any 'new' features, hitherto not defined in the body of the claims, then they should not be allowed but if they are clarificatory or disclaim earlier claimed features, they can be allowed. The relevant observation of the IPAB*

is as under:

> *"36. Keeping in view the settled principles of law, on amendments of the claims, we agree that no new claim may be allowed. But the whole question is whether the claim inserted in "new". Does it define any "new" feature(s) hitherto not defined in the body of the claims? If the answer is 'yes', then such claims are not allowed to be inserted. We refer to the body of the claims as originally filed, and amended subsequently, in both these sets the claim relating to "A composition comprising an isolated antibody or antigen-binding fragment thereof ..." are present. The dependent claims inserted to qualify the features already covered in the principal claims and having sufficient basis in the description cannot be held to be "new". Therefore, we allow the amended set of claims by the appellant except claim 5. We also allow claim 8 for reasons explained in earlier paragraphs.*

54. A perusal of the paragraphs of the Ayyangar Committee Report clearly shows that the purport and intention of this Report was to give broader and wider permissibility for amendment of claims and specification prior to the grant and restrict the same post the grant and advertisement thereof. The Report is also categorical in its observation that the invention before and after amendment need not be identical in case of amendment before acceptance "so long as the invention is comprehended within the matter disclosed.

55. When this standard, as contemplated by the Ayyangar Committee Report, is applied to Section 59 of the Act as it stands today, it becomes clear that amendments to a patent specification or claims prior to grant ought to be construed more liberally rather than narrowly. The purport and spirit of Article 123 of the European Patent Convention is not too different. In effect, the legislative material and the statutory

provisions require that nothing new should be permitted to be inserted in the specification or claims. So long as the invention is disclosed in the specification and the claims are being restricted to the disclosures already made in the specification, the amendment ought not be rejected, especially, at the stage of examination prior to grant."

30. As per the above judgement it is observed that while the amended Claim has disclaimed the earlier broadly claimed feature by defining the necessary amount of composition that is to be used, overall, the amended Claim is not within the scope of the originally filed Claims as the limitation with respect to a specific class of diseases i.e., neurodegenerative diseases has been removed. Accordingly, it is clear that the scope of the Claims before the Court at the stage of appeal are broader than the originally filed Claims as also the Claims of the corresponding PCT application.

Whether the claimed composition results in enhanced therapeutic efficacy?

31. The challenge, however, does not end here. Even if the Court permits the Appellant to reintroduce the limitation in Claim 1 in respect of the neurodegenerative diseases which the composition attempted to cure, the amended Claim would still be hit by non-patentability under Section 3(d) of the Act and enhanced therapeutic efficacy would have to be established to overcome the said refusal.

32. In the context of overcoming objections under Section 3(d) of the Act, the requirement for demonstrating significant enhancement of therapeutic efficacy has been categorically laid down by the Supreme Court in ***Novartis AG v. Union of India, (2013) 6 SCC 1***. The relevant extracts of the said decision are set out below:

"157. What is "efficacy"? Efficacy means "the ability to produce a desired or intended result". Hence, the test of efficacy in the context of section 3(d) would be different, depending upon the result the product under consideration is desired or intended to produce. In other words, the test of efficacy would depend upon the function, utility or the purpose of the product under consideration. Therefore, in the case of a medicine that claims to cure a disease, the test of efficacy can only be "therapeutic efficacy". The question then arises, what would be the parameter of therapeutic efficacy and what are the advantages and benefits that may be taken into account for determining the enhancement of therapeutic efficacy? With regard to the genesis of section 3(d), and more particularly the circumstances in which section 3(d) was amended to make it even more constrictive than before, we have no doubt that the "therapeutic efficacy" of a medicine must be judged strictly and narrowly. ***Our inference that the test of enhanced efficacy in case of chemical substances, especially medicine, should receive a narrow and strict interpretation is based not only on external factors but there are sufficient internal evidence that leads to the same view. It may be noted that the text added to section 3(d) by the 2005 amendment lays down the condition of "enhancement of the known efficacy". Further, the explanation requires the derivative to "differ significantly in properties with regard to efficacy". What is evident, therefore, is that not all advantageous or beneficial properties are relevant, but only such properties that directly relate to efficacy, which in case of medicine, as seen above, is its therapeutic efficacy****.*

158. While dealing with the explanation it must also be kept in mind that each of the different forms mentioned in the explanation have some properties inherent to that form, e. g., solubility to a salt and hygroscopicity to a polymorph. These forms, unless they differ significantly

in property with regard to efficacy, are expressly excluded from the definition of "invention". Hence, the ***mere change of form with properties inherent to that form would not qualify as "enhancement of efficacy" of a known substance****. In other words, the explanation is meant to indicate what is not to be considered as therapeutic efficacy.*

159. We have just noted that the ***test of enhanced therapeutic efficacy must be applied strictly, but the question needs to be considered with greater precision****. In this connection, we take note of two slightly diverging points of view urged before this Court.*

xxx xxx xxx

166. Thus, even if Mr. Grover's submission is not taken into consideration on the question of bioavailability, the position that emerges is that just increased bioavailability alone may not necessarily lead to an enhancement of therapeutic efficacy. ***Whether or not an increase in bioavailability leads to an enhancement of therapeutic efficacy in any given case must be specifically claimed and established by research data.*** *In this case, there is absolutely nothing on this score apart from the adroit submissions of the counsel. No material has been offered to indicate that the beta crystalline form of Imatinib Mesylate will produce an enhanced or superior efficacy (therapeutic) on molecular basis than what could be achieved with Imatinib free base in vivo animal model."*

33. For the said purpose, data relating to sufficient enhancement of therapeutic efficacy would be liable to be assessed. Generally, the complete specification of the patent application, itself, ought to contain the requisite data or references to the requisite data or even results of lab experiments which demonstrate enhancement of efficacy of the subject invention for which patent is sought. The said requirement is in line with the decision by a

ld. Single Judge of this Court, in ***AstraZeneca AB and Ors. v. Intas Pharmaceuticals Limited and Ors., 2020/DHC/3125***, which considered the relevance of post filing data in the context of technical advancement.

34. However, if there is any additional data, such as data from Clinical Trials which becomes available, only post the filing of the patent application, such data may be considered by the patent office as also the Court.

35. In the present case, it is not in doubt that the composition is at best a derivative and would be the same substance as the '*known substance*' under Section 3(d), therefore, unless and until significant enhancement of therapeutic efficacy is shown, such a composition would not be liable to be granted patent protection.

36. As captured in the impugned order as also in the written submissions, the Appellant has tried to argue that the composition in the subject patent is providing enhancement of efficacy. In respect of this submission, reliance is placed upon a press report of the STARS clinical data titled *'Ovid Therapeutic Announces Positive Topline Data from Phase 2 STARS Trial of OV101 for the treatment of Angelman Syndrome'*. The Appellant claims that there has been subsequent enhancement of therapeutic efficacy which shows statistical improvement, observed at 12 weeks of treatment in once daily dose group. The above stated press release for Phase 2 STARS Trial of OV101, which is also freely accessible, seeks to highlight certain advantageous aspects of the compound.

37. However, the Court also observes that results of Phase 3 Trials have not been placed on record which is necessary to determine the efficacy of the said composition. From the publicly available results of the Phase 3 trial

data, it appears that the drug labelled as 'OV 101' for the treatment of Angelman syndrome as also Fragile X Syndrome did not meet the primary endpoints in the respective phase 3 trials. As per publicly available information, as early as in December 2020, the Appellant had announced the results of the Phase 3 trials for the Treatment of Angelman Syndrome[1]. In fact, there are several reports which state that in the Phase 3 clinical trial for Angelman syndrome conducted with 97 children (subjects) who received 'OV101' orally once a day for 12 weeks, the improvement on the subjects was only of 0.7 points on an Angelman scale, however, the placebo group improved by 0.8 points. This clearly is reflecting that the composition for which the subject patent is being sought, is lacking therapeutic efficacy[2].

38. Unfortunately, though a press release of phase 2 trial data has been produced on record, phase 3 data which was available with the Appellant and was also publicly available, has not been produced. Under these circumstances, the appeal is bereft of merit and the patent is not liable to be granted, both due to expansion of the scope of the Claims as also under non-patentability under Section 3(d) of the Act, as there is not enough data to demonstrate significant enhancement of therapeutic efficacy.

39. Appeal is accordingly dismissed. All pending applications if any are also disposed of.

40. Copy of this order be sent to the office of the Controller General of Patents & Trademarks of India on the E-mail: llc-ipo@gov.in. The present

[1] Ovid Therapeutics Announces Phase 3 NEPTUNE Clinical Trial of OV101 for the Treatment of Angelman Syndrome Did Not Meet Primary Endpoint, 1st December, 2020, accesses from: https://www.biospace.com/article/releases/ovid-therapeutics-announces-phase-3-neptune-clinical-trial-of-ov101-for-the-treatment-of-angelman-syndrome-did-not-meet-primary-endpoint/?keywords=Ovid

[2] *Ovid flunks Angelman phase 3, leaving field wide open for rivals*, 2nd December, 2020, accessed from: https://www.fiercebiotech.com/biotech/ovid-flunks-angelman-phase-3-leaving-field-wide-open-for-rivals

judgement be tagged along with the electronic record of the subject patent application

PRATHIBA M. SINGH
JUDGE

FEBRUARY 09, 2024
dj/ks

ANNEXURE 1

1. A method of increasing tonic inhibition of neurons in a subject comprising administering to a human subject with a neurodegenerative disease, a neurogenetic disorder, or a central nervous system disorder a pharmaceutical composition comprising an effective amount of 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase tonic inhibition of neurons of the subject.

2. The method of claim 1 wherein in the subject has Fragile X syndrome Fragile X-associated tremor/ataxia syndrome (FXTAS).

3. The method of claim 1 wherein the subject has Angelman syndrome.

4. A method of treating or preventing Fragile X syndrome or Fragile X associated tremor/ataxia syndrome in a subject comprising administering to a subject with Fragile X syndrome or Fragile X-associated tremor/ataxia a syndrome a pharmaceutical composition comprising an effective amount of 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase tonic inhibition of neurons in the subject.

5. A method of treating or preventing Angelman syndrome in a subject comprising administering to a subject with Angelman syndrome a pharmaceutical composition comprising an effective amount of 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol (THIP) or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase tonic inhibition of neurons in the subject.

6. The method of any one of claims 1-5 wherein the amount of the THIP or derivative thereof is not effective to have an adverse effect in the subject.

7. A method of treating secondary insomnia in a subject comprising administering to a subject with a neurodegenerative disease or a central nervous system disorder a pharmaceutical composition comprising an effective amount of 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridine-3-ol(THIP) or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase slow wave sleep (SWS) and/or slow wave activity (SWA),normalize sleep architecture, reduce secondary insomnia, increase non-rapid eye movement (NREM) sleep, increase sleep continuity, enhance delta activity within NREM, increase or improve total sleep time (TST), increase or improve sleep efficiency, reduce total time awake (TAA), reduce number of awakenings (NWA), reduce latency to persistent sleep (LPS), reduce wake after sleep onset (WASO), or any combination

thereof in the subject.

8. A method of increasing slow wave sleep in a subject comprising administering to a subject with a neurodegenerative disease or a central nervous system disorder a pharmaceutical composition comprising an effective amount of 4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridine-3-ol(THIP) or a derivative thereof and a pharmaceutically acceptable carrier or excipient to increase slow wave sleep in the subject.

9. The method of any of claims 8 or 9 wherein the neurodegenerative disease is selected from the group consisting of Parkinson's Disease (PD)and PD-related disorders, Alzheimer's Disease (AD) and other dementias, Prion Diseases such as Creutzfeldt-Jakob Disease, Corticobasal Degeneration, Frontotemporal Dementia, HIV-Related Cognitive Impairment, Mild Cognitive Impairment, Motor Neuron Diseases (MND),Spinocerebellar Ataxia (SCA), Spinal Muscular Atrophy (SMA), Friedreich's Ataxia, Lewy Body Disease, Alpers' Disease, Batten Disease, Cerebro-Oculo-Facio-Skeletal Syndrome, Corticobasal Degeneration, Gerstmann-Straussler-Scheinker Disease, Kuru, Leigh's Disease, Monomelic Amyotrophy, Multiple System Atrophy, Multiple System Atrophy With Orthostatic Hypotension (Shy-Drager Syndrome), Multiple Sclerosis (MS),Neurodegeneration with Brain Iron Accumulation, Opsoclonus Myoclonus, Posterior Cortical

Atrophy, Primary Progressive Aphasia, Progressive Supranuclear Palsy, Vascular Dementia, Progressive Multifocal Leukoencephalopathy, Dementia with Lewy Bodies, Lacunar syndromes, Hydrocephalus, Wernicke-Korsakoff's syndrome, post-encephalitic dementia, cancer and chemotherapy-associated cognitive impairment and dementia, and depression-induced dementia and pseudodementia.

10. The method of claim 9 wherein the neurodegenerative disease is Huntington's disease.

11. The method of claim 9 wherein the neurodegenerative disease is Parkinson's disease.

12. The method of claim 9 wherein the neurodegenerative disease is Amyotrophic lateral sclerosis.

13. The method of claim 9 wherein the neurodegenerative disease is Alzheimer's disease.

14. The method of any once of claims 7-13 wherein the subject has not been clinically diagnosed with a neurodegenerative disease.

15. The method of any one of claims 7- 13 wherein the subject has no significant physical symptoms of the neurodegenerative

disease, or the clinical symptoms are too mild for an affirmative diagnosis of the neuro degenerative disease.

16. The method of any one of claims 7- 13 wherein the subject has been clinically diagnosed with a neurodegenerative disease.

17. The method of any one of claims 1 - 16 wherein the THIP or derivative thereof is THIP or a pharmaceutically acceptable salt thereof.

18. The method of any one of claims 1 - 17 wherein the THIP or derivative thereof is the singular active agent.

19. The method of any one of claims 1- 18 wherein pharmaceutical composition consists of an effective amount of the THIP or derivative thereof and one or more pharmaceutically acceptable carriers or excipients.

20. The method of any one of claims 1 - 19 wherein the pharmaceutical composition is formulated for extended release.

21. The method of any of claims 1-20 wherein the pharmaceutical composition is administered once every 24-48 hours.

22. The method of any one of claims 1-21 wherein the

pharmaceutical composition is administered transdermally.

23. The method of claim 22 wherein the pharmaceutical composition is administered by contacting a transdermal patch comprising the pharmaceutical composition with the skin of the subject.

24. The method of any one of claims 1-13 wherein the pharmaceutical composition is administered to the subject in the morning or the evening.

25. The method of any one of claims 1-24 wherein the daily dosage of the THIP or derivative thereof is between about 1 mg and 20 mg.

26. The method of any one of claims 1-24, wherein the composition is administered to the subject intravenously.

27. The method of claim 26, wherein the subject is administered a daily dosage of the THIP or derivative thereof is between about 0.001 mg and 30mg.

28. The method of claim 27, wherein the THIP or derivative thereof is administered at a rate of 0.001 mg/kg per hour to 1 mg/kg per hour.

****