

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

To: G.E EHRLICH (1995) LTD. 11 Menachem Begin Road Ramat Gan 5268104 Israel		
		Date of mailing <i>(day/month/year)</i> 04 Apr 2016
Applicant's or agent's file reference 64402		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/IL2015/051193	International filing date <i>(day/month/year)</i> 09 Dec 2015	Priority date <i>(day/month/year)</i> 09 Dec 2014
International Patent Classification (IPC) or both national classification and IPC IPC (2016.01) C07C 211/42 C07C 309/66 C07D 295/096 C07D 317/70 C07D 319/18		
Applicant GOLAN Ezekiel		

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Facsimile No. 972-2-5651616	Date of completion of this opinion 03 Apr 2016	Authorized officer VOLKOV Karina Telephone No. 972-2-5651777
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WRITTEN OPINION OF THE
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International application No.
PCT/IL2015/051193

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - the international application in the language in which it was filed.
 - a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. forming part of the international application as filed:
 - in the form of an Annex C/ST.25 text file.
 - on paper or in the form of an image file.
 - b. furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. furnished subsequent to the international filing date for the purposes of international search only:
 - in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).
 - on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).
4. In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>2-11,22-38</u>	YES
	Claims <u>1,12-21</u>	NO
Inventive step (IS)	Claims	YES
	Claims <u>1-38</u>	NO
Industrial applicability (IA)	Claims <u>1-38</u>	YES
	Claims	NO

2. Citations and explanations:

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Reference is made to the following documents:

D1 US 5708018(A) UPJOHN CO [US] 1998-01-13

D2 VENGELIENE, Valentina, et al. The dopamine D3 receptor plays an essential role in alcohol-seeking and relapse. The FASEB journal, 2006, 20.13: 2223-2233.

2.1 Novelty:

The present claims do not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1,12-21 is not novel in the sense of Article 33(2) PCT.

D1 discloses 2-aminoindan analogs that selectively bind to dopamine D3 receptor which may be useful in treating CNS disorders, e.g. schizophrenia, mania, depression, geriatric disorders, drug abuse and addiction, Parkinson's disease, anxiety disorders, sleep disorders, circadian rhythm disorders and dementia. The dopamine D3 receptor is of importance for the action of anti-psychotics and shows a high abundance in brain regions associated with emotional and cognitive functions.

Since, D1 exemplified compound 5-Flouro-2-(di-n-propylamino)indan (column 12) which is overlap with compounds disclosed in claim 1 of the present application and known for use in drug addition, nothing new can be seen in the subject-matter of claims 1.

The dependent claims 12-21 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT with respect to novelty PCT Article 33(2) PCT.

Although D1 describes 2-aminoindan analogs as described in claim 1 useful in drug abuse and addiction it does not describe using said compounds in method for regulating a drinking binge behavior, as claimed in claim 2.

Therefore, claims 2-3 of present application meet the criteria of Article 33(2) PCT.

Independent claim 4 relates to a method of regulating consumption of an alcoholic beverage, the method comprising administering to a subject in need thereof a compound represented by Formula I as claimed in claim 1. Although D1 describes 2-aminoindan analogs as described in claim 1 useful in drug abuse and addiction it does not describe a method of regulating consumption of an alcoholic beverage, as claimed in claim 4.

Therefore, claims 4-11 of present application meet the criteria of Article 33(2) PCT.

Independent claim 22 relates to a compound represented by Formula I as defined in claim 1 for use in regulating binge behavior. Although D1 describes 2-aminoindan analogs as described in claim 1 useful in drug abuse and addiction it does not describe said compound for use in regulating binge behavior .

Therefore, claims 22-38 of present application meet the criteria of Article 33(2) PCT.

2.2 Inventive Step:

The present claims do not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-48 does not fulfill the requirements of Article 33(3) PCT.

The subject-matter of claims 1,12,13 is not considered to involve an inventive step (Article 33 (3) PCT) for the reasons mentioned above (not novel).

D1 discloses 2-aminoindan analogs that selectively bind to the dopamine D3 receptor. The dopamine D3 receptor is of importance for the action of anti-psychotics and shows a high abundance in brain regions associated with emotional and cognitive functions. 2-aminoindan analogs may be useful in treating CNS disorders, e.g. schizophrenia, mania, depression, geriatric disorders, drug abuse and addiction, Parkinson's disease, anxiety disorders, sleep disorders, circadian rhythm disorders and dementia.

D1 mentions (column3 lines 59-62) that the compound of Formula I can be given in the amount of about 0.25-100 mg per person.

Furthermore, it is known from D1 that these compounds can be given orally, as liquid dosage forms such as elixirs, syrups or suspensions and solid dosage form such tablet. (column 3 lines 52-55).

D2 discloses the blockade of dopamine D3Rs receptor subtype can reduce alcohol-seeking and relapse behavior. D2 mentions that the increase in dopamine release was seen in the dorsal striatum during alcohol-seeking behavior and blockade of dopamine receptors within the dorsal striatum decreased alcohol seeking.

D2 indicates that the effect of the dopamine D3R ligands was selective for alcohol. It appears to be that the crucial receptor in mediating dopamine dependent processes related to alcohol craving and relapse in the dopamine D3R .

Claim 2 refers to a method of regulating binge behavior which associated with alcohol consumption, eating, tobacco consumption, shopping or sexual conduct.

The method comprising administrating to a subject in need thereof a compound represented by Formula I claimed in claim 1.

Claim 2 lacks an inventive step under Article 33(3) PCT as being obvious over D1 in view of D2. Document D1 discloses 2-aminoindan derivatives for treating central nervous system (CNS) disorders associated with the dopamine D3 receptor activity, such as drug abuse and addiction. Document D2 teaches that the blockade of dopamine D3Rs receptor subtype can reduce alcohol-seeking and relapse behavior .

In view of these teachings, it would have been obvious to one of ordinary skill in the art to provide a method for regulating binge behavior by administrating to a subject in need thereof a compound of 2-aminoindan represented by Formula I in claim 1.

None of the features of dependent claims 3-38 based on the prior art cited (see D1-D2) seem to have any surprising technical effect as regards an inventive step.

Therefore the subject matter of claims 2-38 is not considered inventive (Article 33(3)PCT).

2.3 Industrial applicability

The subject-matter of claims 1-38 is considered to be industrially applicable in the sense of Article 33(4) PCT.

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International application No.

PCT/IL2015/051193

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The wording "All publication ... incorporated by reference" on page 43-44 lines 29-2 seeks to extend the scope of protection sought in some vague and indefinite manner and, therefore should be amended.