

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:

100080
China 10th Floor, Building 1, 10 Caihefang Road,
Haidian District, Beijing

LIU, SHEN & ASSOCIATES

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference F19W5610		Date of mailing (day/month/year) 05 February 2020
FOR FURTHER ACTION See paragraph 2 below		
International application No. PCT/CN2019/119373	International filing date (day/month/year) 19 November 2019	Priority date (day/month/year) 22 November 2018
International Patent Classification (IPC) or both national classification and IPC C07D 401/04(2006.01)i; C07D 405/04(2006.01)i; C07D 487/04(2006.01)i; A61K 31/497(2006.01)i; A61K 31/4427(2006.01)i; A61P 3/10(2006.01)i		
Applicant QILU REGOR THERAPEUTICS INC. et al		

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 43bis.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 66.1bis(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/ National Intellectual Property Administration, PRC China 6, Xitucheng Rd., Jimen Bridge, Haidian District, Beijing 100088	Date of completion of this opinion 20 January 2020	Authorized officer QIN,Xue
Facsimile No. (86—10) 62019451		Telephone No. 86-(10)-53962164

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. I

Basis of the 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 43bis.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 13ter.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 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.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:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 39

because:

☒ the said international application, or the said claims Nos. 39 relate to the following subject matter which does not require an international search (*specify*):

[1] Claim 39 relates to a method of treating diseases, but the opinion has been carried out based on use of the compounds in the manufacture of medicaments for treating the alleged diseases.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☐ no international search report has been established for said claims Nos. _____

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

☐ See Supplemental Box for further details.

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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	1-40	YES
	Claims	None	NO
Inventive step (IS)	Claims	14-16, 24, 28	YES
	Claims	1-13, 17-23, 25-27, 29-40	NO
Industrial applicability (IA)	Claims	1-40	YES
	Claims	None	NO

2. Citations and explanations :

[1] 2.1 Cited documents

[2] D1: WO 2018109607A1

[3] D2: WO 2013090454A2

[4] D3: WO 2011143365A1

[5] 2.2 Novelty

[6] D1 (see abstract, description, page 17, line 10 to page 19, line 9, examples IA-14A, claims 1, 23-24) discloses compounds of formula I as GLP-1 R agonist, a pharmaceutical composition thereof, and a method of treating cardiometabolic and associated diseases with said compounds. The compounds of present claim 1 differ from the compounds of examples 1A-14A in D1 in that present claim 1 excludes the compounds of D1.

[7] D2 (see abstract, claims 1-33) discloses compounds that modulate GLP-1 receptor, and their therapeutic use.

[8] D3 (see abstract, claims 1-25) discloses compounds as PDE10 inhibitor and their therapeutic use.

[9] Claims 1-40 are not disclosed by D1-D3. Therefore, claims 1-40 are novel in the sense of PCT Article 33(2).

[10] 2.3 Inventive step

[11] With regard to claim 1, D1 is regarded as the closest prior art. The difference between claim 1 and D1 is as mentioned above. The problem to be solved by the present invention is providing further compounds with GLP-1 R agonist activity.

[12] However, it is obvious to a person skilled in the art to arrive at formula I through bioisostere replacement. Therefore, claim 1 does not involve an inventive step in the sense of PCT Article 33(3).

[13] The additional features of the dependent claims 2-13,17-23,25-27,29-40 are either disclosed by D1, or common selections in the art. Therefore, claims 2-13,17-23,25-27,29-40 do not involve an inventive step in the sense of PCT Article 33(3).

[14] Claims 14-16 involve an inventive step, because the prior art does not teach or fairly suggest that ring B may form a bicyclic structure.

[15] Claims 24,28 involve an inventive step, because the prior art does not teach or fairly suggest that ring C may select the structure which described in the present Claims 24,28.

[16] As compounds according to claims 1-13, 17-23,25-27,29-37 do not involve an inventive step, claims 38-40 do not involve an inventive step.

[17] 2.4 Industrial applicability

[18] Claims 1-40 can be made or used in pharmaceutical industry. Therefore, claims 1-40

[19] Meet the criteria set out in PCT Article 33(4).

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

- [1] The multiple dependent claims 4-6, 8-13, 17-22, 26-36 refer to preceding multiple dependent claims. Therefore, these claims do not meet the criteria set out in PCT Rule 6.4(a).