PATENT COOPERATION TREATY **TRANSLATION**

From the INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)* **03 August 2017**
Applicant's or agent's file reference **IEC170031PCT**	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CN2017/087433	**07 June 2017**	**08 June 2016**

International Patent Classification (IPC) or both national classification and IPC
C07D 471/04(2006.01)i; A61K 31/4545(2006.01)i; A61P 3/10(2006.01)i; A61P 3/06(2006.01)i; A61P 5/48(2006.01)i

Applicant
XUANZHU PHARMA CO., LTD.

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/	Date of completion of this opinion	Authorized officer

TRANSLATION

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CN2017/087433

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 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 filed or furnished:
   a. (means)
      - ☐ on paper
      - ☐ in electronic form
   b. (time)
      - ☐ in the international application as filed
      - ☐ together with the international application in electronic form
      - ☐ subsequently to this Authority for the purposes of search

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 in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

TRANSLATION

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CN2017/087433

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. **12**

because:

☑ the said international application, or the said claims Nos. **12** relate to the following subject matter which does not require an international search *(specify)*:

[1] Claim 12 relates to a method for treating diseases. However, in this statement, the examination is made on the basis of the corresponding pharmaceutical use of the compound of the present application.

☐ 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 on paper 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 a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form 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 a form and manner acceptable to it.

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

☐ See Supplemental Box for further details.

TRANSLATION

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CN2017/087433

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**

1. Statement

Novelty (N)	Claims	1-13	YES
	Claims	None	NO
Inventive step (IS)	Claims	None	YES
	Claims	1-13	NO
Industrial applicability (IA)	Claims	1-13	YES
	Claims	None	NO

2. Citations and explanations :

[1] 2.1. Cited documents

[2] D1: CN 102127072 A (Shandong Xuanzhu Pharma Co., Ltd.), 20 July 2011 (20.07.2011)

[3] D2: CN 102863440 A (Shandong Xuanzhu Pharma Co., Ltd.), 09 January 2013 (09.01.2013)

[4] D3: SHU, Chutian et al., "Discovery of Imigliptin, a Novel Selective DPP-4 Inhibitor for the Treatment of Type 2 Diabetes", ACS Medicinal Chemistry Letters, no. 8, vol. 5, 16 June 2014 (16.06.2014), pp. 921-926

[5] 2.2. Novelty

[6] D1 discloses a trifluoroacetate of compound 17 (i.e. formula (I) in claim 1) and a preparation method therefor (description, example 17).

[7] D2 discloses a dihydrochloride crystal form I of the compound of formula (1) (claim 1).

[8] D3 discloses a compound 27 (page 925, Scheme 1.).

[9] None of D1 to D3 discloses a succinate crystal of the compound of formula (I) of claim 1. Therefore, claim 1 is novel and complies with PCT Article 33(2).

[10] D1 to D3 likewise do not disclose the subject matter of claims 2-13. Therefore, claims 2-13 are likewise novel and comply with PCT Article 33(2).

[11] 2.3. Inventive Step

[12] With regard to claim 1, D1 is the closest prior art. Then, the crystalline salt of claim 1 differs from the salt disclosed in D1 in respect of the type of an acid for forming a salt with the compound of formula (I). The technical problem to be actually solved by claim 1 is to provide a succinate crystal of the compound of formula (I). However, it is a conventional technical means in the art to prepare a pharmaceutical compound into various common salts and then to obtain a crystal by purification, and succinic acid is an organic acid conventionally used in the art to form a salt with a drug. Therefore, on the basis of D1, it would have been obvious to a person skilled in the art to arrive at the technical solution in claim 1. Hence, claim 1 does not involve an inventive step and does not comply with PCT Article 33(3). On the basis of the same reasoning, claims 2-4 and 13 likewise do not involve an inventive step and do not comply with PCT Article 33(3).

[13] With regard to claim 5, D1 discloses, in example 17, a method for preparing the trifluoroacetate of compound 17. Then, claim 5 differs from D1 in respect of the type of the salt and the specific operation for crystallization. The technical problem to be actually solved by claim 5 is to provide a method for preparing a succinate salt of the compound of formula (I). However, when preparing a specific salt of a compound, a person skilled in the art would have been motivated to combine an acid reaction to the operation of example 17 of D1, and perform solvent selection and the optimization of the operation steps according to common technical knowledge and experimental means known thereby. Hence, claim 5 does not involve an inventive step and does not comply with PCT Article 33(3). On the basis of the same reasoning, claims 6-9 likewise do not involve an inventive step and do not comply with PCT Article 33(3).

[14] Claim 10 sets forth a pharmaceutical composition. Claims 11 and 12 set forth the pharmaceutical use of the compound. D1 discloses a composition comprising the compound thereof and a corresponding

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**

pharmaceutical use thereof (claims 10 and 11). Therefore, claims 10-12 likewise do not involve an inventive step and do not comply with PCT Article 33(3).

[15] 2.4. Industrial Applicability

[16] Claims 1-13 can be made or used in the pharmaceutical industry, and thus are industrially applicable in the sense of PCT Article 33(4).

TRANSLATION

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/CN2017/087433

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:

[1] The use of "preferably" in claim 1 renders that the claim defines different scope of protection. Claim 1 does not comply with PCT Article 6.