

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

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IPT DOCKETING

Docketed ☐ Not Docketed ☐ Confirmation ☐

SEP 05 2019

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference REAT.P0103WO Docket No. _____	Date of mailing (day/month/year) 2 September 2019 (02-09-2019)
International application No. PCT/US2019/037543	FOR FURTHER ACTION See paragraphs 1 and 4 below International filing date (day/month/year) 17 June 2019 (17-06-2019)
Applicant REATA PHARMACEUTICALS, INC.	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.

How? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70

For more detailed instructions, see PCT Applicant's Guide, International Phase, paragraphs 9.004 - 9.011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

Shortly after the expiration of **18 months from the priority date**, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, within **20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide, National Chapters*.

Within **22 months from the priority date**, the applicant may request that a supplementary international search be carried out by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide, International Phase, paragraphs 8.006-8.032*.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel: (+31-70) 340-2040 Fax: (+31-70) 340-3016	Authorized officer CURRIE, Susan Tel: +49 (0)89 2399-8031
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference REAT P0103WO	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2019/037543	International filing date (day/month/year) 17 June 2019 (17-06-2019)	(Earliest) Priority Date (day/month/year) 15 June 2018 (15-06-2018)
Applicant REATA PHARMACEUTICALS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out 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))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No. III)

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____
☐ as suggested by the applicant
☐ as selected by this Authority, because the applicant failed to suggest a figure
☐ as selected by this Authority, because this figure better characterizes the invention
 b. ☐ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/037543

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D401/14 C07D413/14 C07D231/54 C07D401/04 C07D235/02
 C07D401/10 C07D403/04 C07D403/10 C07D405/04 C07D409/04
 C07D413/04 C07D413/10 C07D417/04 A61P29/00 A61K31/416

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2016/130927 A1 (REATA PHARMACEUTICALS INC [US]) 18 August 2016 (2016-08-18) page 48 - page 54; claims; examples -----	1-175
X	HUERTA CARLOS ET AL: "Characterization of novel small-molecule NRF2 activators: Structural and biochemical validation of stereospecific KEAP1 binding", BIOCHIMICA ET BIOPHYSICA ACTA (BBA) - GENERAL SUBJECTS, ELSEVIER, AMSTERDAM, NL, vol. 1860, no. 11, 27 July 2016 (2016-07-27), pages 2537-2552, XP029708201, ISSN: 0304-4165, DOI: 10.1016/J.BBAGEN.2016.07.026 the whole document ----- -/-	1-175



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier application or patent but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

& document member of the same patent family

Date of the actual completion of the international search

22 August 2019

Date of mailing of the international search report

02/09/2019

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040,
 Fax: (+31-70) 340-3016

Authorized officer

Gavriliu, Daniela

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/037543

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2015/112792 A1 (ABBVIE INC [US]; REATA PHARMACEUTICALS INC [US]) 30 July 2015 (2015-07-30) page 63 - page 75; claims; examples -----	1-175
X	WO 2012/083306 A2 (REATA PHARMACEUTICALS INC [US]; ANDERSON ERIC [US] ET AL.) 21 June 2012 (2012-06-21) page 41 - page 101; claims; examples -----	1-175

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/037543

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2016130927 A1	18-08-2016	AU 2016219109 A1 BR 112017017133 A2 CA 2974726 A1 CN 107428698 A EA 201791814 A1 EP 3256451 A1 JP 2018505196 A KR 20170117092 A US 2018127380 A1 WO 2016130927 A1	24-08-2017 03-04-2018 18-08-2016 01-12-2017 29-12-2017 20-12-2017 22-02-2018 20-10-2017 10-05-2018 18-08-2016
WO 2015112792 A1	30-07-2015	CA 2936550 A1 CN 107074801 A EP 3097089 A1 JP 6530758 B2 JP 2017503840 A TW 201605808 A US 2015225397 A1 WO 2015112792 A1	30-07-2015 18-08-2017 30-11-2016 12-06-2019 02-02-2017 16-02-2016 13-08-2015 30-07-2015
WO 2012083306 A2	21-06-2012	AR 084353 A1 AU 2011343466 A1 CA 2822071 A1 CL 2013001754 A1 CN 103596929 A CO 6910185 A2 CY 1120032 T1 DK 2651902 T3 EA 201390894 A1 EP 2651902 A2 ES 2653717 T3 HK 1189595 A1 HR P20171859 T1 HU E038046 T2 IL 226923 A JP 5857068 B2 JP 2014501250 A KR 20130130784 A LT 2651902 T ME 02973 B NO 2651902 T3 NZ 612788 A PL 2651902 T3 PT 2651902 T SG 191181 A1 SI 2651902 T1 TW 201249785 A US 2012196880 A1 US 2014051739 A1 US 2016130220 A1 US 2018265455 A1 WO 2012083306 A2 ZA 201305060 B	08-05-2013 25-07-2013 21-06-2012 29-11-2013 19-02-2014 31-03-2014 12-12-2018 08-01-2018 30-12-2013 23-10-2013 08-02-2018 04-08-2017 26-01-2018 28-09-2018 30-06-2016 10-02-2016 20-01-2014 02-12-2013 10-01-2018 20-07-2018 07-04-2018 30-10-2015 30-04-2018 01-02-2018 31-07-2013 28-02-2018 16-12-2012 02-08-2012 20-02-2014 12-05-2016 20-09-2018 21-06-2012 27-07-2016

Information on Search Strategy - Pilot phase (see OJ 2015, A86)

The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number

PCT/US2019/037543

TITLE: PYRAZOLE AND IMIDAZOLE COMPOUNDS FOR INHIBITION OF IL-17 AND RORGAMMA

APPLICANT: REATA PHARMACEUTICALS, INC.

IPC CLASSIFICATION: C07D401/14, C07D413/14, C07D231/54, C07D401/04, C07D235/02, C07D401/10, C07D403/04, C07D403/10, C07D405/04, C07D409/04, C07D413/04, C07D413/10, C07D417/04, A61P29/00, A61K31/416, A61K31/4184

EXAMINER: Gavrilu, Daniela

CONSULTED DATABASES: DOSYS, EPODOC, WPI, REGISTRY, CAPLUS, REAXYS, NPL

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: C07D401/14, C07D413/14, C07D231/54, C07D401/04, C07D235/02, C07D401/10, C07D403/04, C07D403/10, C07D405/04, C07D409/04, C07D413/04, C07D413/10, C07D417/04, A61P29/00

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:

Naphthopyrazole and naphthoimidazole derivatives useful to treat diseases connected to the inhibition of IL-17 and ROR gamma

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2019/037543

International filing date (day/month/year)
17.06.2019

Priority date (day/month/year)
15.06.2018

International Patent Classification (IPC) or both national classification and IPC

INV. C07D401/14 C07D413/14 C07D231/54 C07D401/04 C07D235/02 C07D401/10 C07D403/04 C07D403/10
C07D405/04 C07D409/04 C07D413/04 C07D413/10 C07D417/04 A61P29/00 A61K31/416 A61K31/4184

Applicant
REATA PHARMACEUTICALS, INC.

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 usually 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:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0
Fax: +49 89 2399 - 4465

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Gavriliu, Daniela

Telephone No. +49 89 2399-0



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:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2019/037543

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

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	<u>1-175</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-175</u>
Industrial applicability (IA)	Yes: Claims	<u>1-175</u>
	No: Claims	

2. Citations and explanations

see separate sheet

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:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

- D1 WO 2016/130927 A1
- D2 HUERTA CARLOS ET AL: "Characterization of novel small-molecule NRF2 activators: Structural and biochemical validation of stereospecific KEAP1 binding", BIOCHIMICA ET BIOPHYSICA ACTA (BBA) - GENERAL SUBJECTS, ELSEVIER, AMSTERDAM, NL, vol. 1860, no. 11, 27 July 2016 (2016-07-27), pages 2537-2552, XP029708201, ISSN: 0304-4165, DOI: 10.1016/J.BBAGEN.2016.07.026
- D3 WO 2015/112792 A1
- D4 WO 2012/083306 A2

2 Independent claims:

- compounds claims (claim 1 and 141)
- their pharmaceutical compositions (claim 142)
- their pharmaceutical uses (claim 150)

3 For the assessment of the present claims 150-175 on the question whether they are industrial applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may also allow, however, claims to a known compound for the manufacture of a medicament for a new medical treatment.

4 Novelty (Article 33(1) and (2) PCT)

D1 to D4 disclose specific compounds (see the examples of D1, the compounds disclosed on page 2542 of D2 and the D3-D4 examples containing a benzo[g]indazol core-ring) which fall under the scope of current claim 1. In addition, the general structures of D1, D3 and D4 present overlapping region with the general structure claimed by the current set of claims.

Thus, the present claimed subject-matter appear not to fulfill the requirements of Article 33(1) and (2) PCT.

5 Inventive step (Article 33(1) and (3) PCT)

For the potential novel subject-matter the following observations are put forward:

The present compounds, potential novel, are to be seen as a novel selection from the general structures disclosed in D1, D3-D4. The documents D1 to D4 disclose compounds having anti-inflammatory activity and which activate the NRF2 (the same activation is disclosed also for the present compounds). Such a selection can only be regarded as inventive if the compounds of formula (I) present unexpected effects or properties in relation to the rest of compounds disclosed in the prior art. Since no such effects or properties are indicated and supported in the application, the potential novel subject-matter does not involve an inventive step within the meaning of Article 33(1) and (3) PCT. In addition, it is pointed out that data showing activity for an extra receptor (which was not specifically mentioned in the prior art) cannot be considered as involving an inventive step since firstly for establishing inventive step relevant is the pharmacological effect and not the mechanism of action and secondly since the compounds of D1-D4 are disclosed to be anti-inflammatory agents they could also be implicitly inhibitors of IL-17 and ROR gamma.

Re Item VIII

Certain observations on the international application

- 1 Current claim 142 appears to claim specific compounds which fall under the scope of claim 1. Thus, in order to fulfill the requirements of Article 6 PCT claim 142 should be dependent on claim 1.

- 2 It is pointed out that in view of the D1-D4 disclosures, directed to compounds falling under the scope of claim 1 and having the same pharmacological uses, it is not clear which is the common technical feature which could be seen as an unifying feature for the potential novel subject-matter.

Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO/ISA)

General information

For all international applications, the competent International Searching Authority (ISA) will establish an international search report (ISR) accompanied by a written opinion of the International Searching Authority (WO/ISA). The WO/ISA may be responded to by

- filing informal comments with the International Bureau of WIPO (IB) (where no demand for international preliminary examination (**demand**) is filed)
- filing amendments under Art. 19 PCT (this can be done whether or not a **demand** is filed)
- filing amendments under Art. 34 PCT and/or formal observations in response to objections raised in the WO/ISA (where a **demand** is actually filed)

This document explains these possibilities.

Filing informal comments

After receipt of the **ISR** and **WO/ISA**, the applicant may file informal comments on the **WO/ISA**, **directly with the IB** (see International Search and Preliminary Examination Guidelines 2.15). These will be communicated to the designated/elected Offices, together with the International Preliminary Report on Patentability (**IPRP**) at 30 months from the priority date.

Amending claims under Art. 19 PCT

The applicant may file **amended claims** under Art. 19 PCT, **directly with the IB** by the later of the following dates:

- 2 months from the date of mailing of the **ISR** and the **WO/ISA**
- 16 months from the priority date

However, any such amendment received by the **IB** after the expiration of the applicable time limit shall be **considered to have been received on time** by the **IB**, if it reaches it **before** the technical preparations for international publication have been completed (the 15th day prior to the date of publication, see PCT Applicant's Guide, International Phase, 9.013).

For further information, please see Rule 46 PCT as well as form PCT/ISA/220.

Please also note that, when filing amended claims under Art. 19 PCT, such amendments shall be **accompanied by a letter** identifying the amendments made and also the basis for the amendments in the application as originally filed (Rule 46.5(b) PCT). Where a **demand** is filed, failure to comply with this requirement may result in the amendments being ignored in the International Preliminary Examination Report (**IPER**), see Rule 70.2(c-bis) PCT.

Bitte beachten Sie, dass angeführte Nichtpatentliteratur (wie z. B. wissenschaftliche oder technische Dokumente) je nach geltendem Recht dem Urheberrechtsschutz und/oder anderen Schutzarten für schriftliche Werke unterliegen könnte. Die Vervielfältigung urheberrechtlich geschützter Texte, ihre Verwendung in anderen elektronischen oder gedruckten Publikationen und ihre Weitergabe an Dritte ist ohne ausdrückliche Zustimmung des Rechtsinhabers nicht gestattet.

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