

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 10275-0223-00304	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2023/071721	International filing date (<i>day/month/year</i>) 4 August 2023 (04-08-2023)	(Earliest) Priority Date (<i>day/month/year</i>) 4 August 2022 (04-08-2022)
Applicant VERTEX PHARMACEUTICALS INCORPORATED		

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 6 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

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: **1-43 (partially)**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims;; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

International application No
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A. CLASSIFICATION OF SUBJECT MATTER		
INV.	A61K9/16 A61K9/14 A61K9/20 A61K31/404 A61K31/4439 A61K31/47 A61P11/00	
ADD.		
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) A61K 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, 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	Anonymous: "HIGHLIGHTS OF PRESCRIBING INFORMATION - TRIKAFTA", , 1 June 2021 (2021-06-01), pages 1-18, XP093100684, Retrieved from the Internet: URL:https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212273s0041b1.pdf [retrieved on 2023-11-13]	1-43
Y	page 1, left-hand column, paragraphs Indications, Dosage forms pages 7-8, paragraph 11 -----	1-43
Y	WO 2020/242935 A1 (VERTEX PHARMA [US]) 3 December 2020 (2020-12-03) paragraphs [0137] - [0151], [0156]; claims 1-8; example 4 ----- --/--	1-43
☒ 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 14 November 2023		Date of mailing of the international search report 06/12/2023
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 Madalinska, K

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2019/152940 A1 (VERTEX PHARMA [US]) 8 August 2019 (2019-08-08) claims 1-61	1-43
T	----- KAUSHIKA PATEL ET AL: "Solid dispersion technology as a formulation strategy for the fabrication of modified release dosage forms: A comprehensive review", DARU JOURNAL OF PHARMACEUTICAL SCIENCES, BIOMED CENTRAL LTD, LONDON, UK, vol. 30, no. 1, 18 April 2022 (2022-04-18) , pages 165-189, XP021302810, DOI: 10.1007/S40199-022-00440-0 table 2	
T	----- BHUJBAL SONAL V. ET AL: "Pharmaceutical amorphous solid dispersion: A review of manufacturing strategies", ACTA PHARMACEUTICA SINICA B, vol. 11, no. 8, 1 August 2021 (2021-08-01) , pages 2505-2536, XP055881096, ISSN: 2211-3835, DOI: 10.1016/j.apsb.2021.05.014 table 1	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2020242935	A1	03-12-2020	NONE
WO 2019152940	A1	08-08-2019	AU 2019215231 A1 13-08-2020
		BR 112020014487 A2	01-12-2020
		CA 3088272 A1	08-08-2019
		CN 111818918 A	23-10-2020
		EP 3749301 A1	16-12-2020
		IL 275982 A	31-08-2020
		JP 7373491 B2	02-11-2023
		JP 2021512117 A	13-05-2021
		MA 51739 A	16-12-2020
		RU 2020129238 A	10-03-2022
		TW 201944994 A	01-12-2019
		US 2019240197 A1	08-08-2019
		US 2022257564 A1	18-08-2022
		WO 2019152940 A1	08-08-2019

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-43 (partially)

Present independent claims 1, 24, 25, 26, 27, 28 relates to an extremely large number of possible compounds hidden by the names compound I, Compound II and Compound III. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a very small proportion of the compounds I, II and III claimed - see e.g. [009], [0053], [0054], [0058]-[0061] and examples 1-9, namely for:

- a Compound

I being only

N-(1,3-dimethylpyrazol-4-yl)sulfonyl-6-[3-(3,3,3-trifluoro-2,2-dimethyl-propoxy)pyrazol-1-yl]-2-[(4S)-2,2,4-trimethylpyrrolidin-1-yl]pyridine-3-carboxamide

- a Compound II being only

(R)-1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-N(1-(2,3-dihydroxypropyl)-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl)cyclopropanecarboxamide (tezacaftor)

- a Compound III being only

N (5-hydroxy-2,4-di-tert-butyl-phenyl)-4-oxo-1H-quinoline-3-carboxamide (ivacaftor).

The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 1-42 (PCT Guidelines 9.19 and 9.23).

The search of claims 1-42 was thus restricted to those claimed compounds I, II, III, which appear to be supported, namely for the specific compounds I-III as mentioned above and defined in [0009], [0053], [0054], [0058]-[0061].

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) PCT declaration be overcome.