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DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

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Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:

11 August 2022 (11.08.2022)

(54) Title: BENZENESULFONAMIDE DERIVATIVES AND USES THEREOF

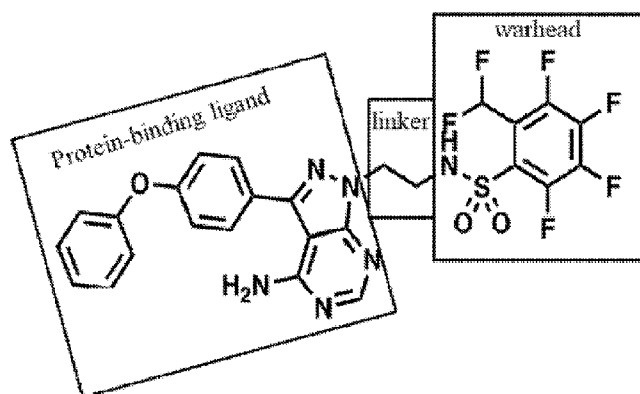


FIG. 20

(57) Abstract: Provided herein are benzenesulfonamide compounds, pharmaceutical compositions comprising said compounds, and methods for using said compounds for the treatment of diseases.



INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2021/000813

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D239/48 C07D403/12 C07D405/12 C07D487/04 C07C307/10
A61K31/506 A61K31/519 A61P35/00

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)

C07D

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, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|------------------------------------------------------------------------------------|-----------------------|
|-----------|------------------------------------------------------------------------------------|-----------------------|

X

LINKUVIENE VAIDA ET AL: "Introduction of Intrinsic Kinetics of Protein-Ligand Interactions and Their Implications for Drug Design", JOURNAL OF MEDICINAL CHEMISTRY, vol. 61, no. 6, 21 February 2018 (2018-02-21), pages 2292-2302, XP055895738, US ISSN: 0022-2623, DOI: 10.1021/acs.jmedchem.7b01408 page 2292; figures 1, 6

**1-48,
79-83**

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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

13 May 2022

Date of mailing of the international search report

15/07/2022

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/000813

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.: **1-83 (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:

see additional sheet

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.:
1-48 (completely) ; 79-83 (partially)

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 SEARCH REPORT

International application No

PCT/IB2021/000813

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | <p>CASINI ANGELA ET AL: "Cysteine-Modifying Agents: A Possible Approach for Effective Anticancer and Antiviral Drugs", ENVIRONMENTAL HEALTH PERSPECTIVES, vol. 110, no. 5, 1 October 2002 (2002-10-01), pages 801-806, XP055784146, abstract; compounds 8-12, 14, 15</p> <p>-----</p> | 1-48, 79-83 |
| X | <p>YANG JIANHONG ET AL: "Cysteine-Modifying Agents: A Possible Approach for Effective Anticancer and Antiviral Drugs", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 294, no. 20, 1 May 2019 (2019-05-01), pages 8161-8170, XP055784148, US ISSN: 0021-9258, DOI: 10.1074/jbc.RA118.006325 abstract; compound T138067</p> <p>-----</p> | 1-48, 79-83 |
| X | <p>WO 00/35865 A2 (TULARIK INC [US]) 22 June 2000 (2000-06-22) claims; examples</p> <p>-----</p> | 1-48, 79-83 |
| X | <p>WO 98/05315 A1 (TULARIK INC [US]) 12 February 1998 (1998-02-12) claims; examples</p> <p>-----</p> | 1-48, 79-83 |
| X | <p>MEDINA J C ET AL: "Novel halogenated sulfonamides inhibit the growth of multidrug resistant MCF-7/ADR cancer cells", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, ELSEVIER, AMSTERDAM, NL, vol. 9, no. 13, 5 July 1999 (1999-07-05), pages 1843-1846, XP004168849, ISSN: 0960-894X, DOI: 10.1016/S0960-894X(99)00276-0 scheme 1; table 1; abstract</p> <p>-----</p> | 1-48, 79-83 |
| X | <p>SHAN B. ET AL: "Selective, covalent modification of α-tubulin residue Cys-239 by T138067, an antitumor agent with in vivo efficacy against multidrug-resistant tumors", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 96, no. 10, 11 May 1999 (1999-05-11), pages 5686-5691, XP055784141, ISSN: 0027-8424, DOI: 10.1073/pnas.96.10.5686 figure 1, compound A; abstract</p> <p>-----</p> | 1-48, 79-83 |
| | ----- -/-- | |

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2021/000813

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| X | <p>WO 2012/101239 A1 (PF MEDICAMENT [FR]; KALOUN EL BACHIR [FR] ET AL.) 2 August 2012 (2012-08-02) cited in the application claims; examples</p> <p>-----</p> | <p>1-48, 79-83</p> |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-48(completely); 79-83(partially)

A compound of formula (I) and its use

2. claims: 49-78(completely); 79-83(partially)

A compound of formula (I-A) and its use

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-83(partially)

Present claims 1-83 relate to an extremely large number of possible compounds, compositions, proteins, methods due to the fact that formulas (I) and (IA) of present claims contain so many options and variables with respect to the definitions of G, G 1, L2, D1, L, D2. 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, compositions, proteins, methods claimed, see the examples.

The compounds of formulas (I) and (IA) are defined by functional features, namely "protein-binding ligand", "radical of a protein-binding ligand", "warhead radical", "covalently modifies a target protein" etc., contrary to the requirements of clarity of Article 6 PCT, because the result-to-be-achieved type of definition does not allow the scope of the claim to be ascertained.

These functional features defining the result to be achieved in connection with indefinite structural features, as is the case here, cannot assist in rendering a claim clear, since it still leaves open what exactly the subject-matter is for which patent protection is now claimed. Furthermore such a claim would impose a severe and undue burden on all those wishing to ascertain the scope of the exclusive right (e.g. the public and the third parties), which would be contrary to Article 6 PCT which requires that the claims shall define the matter for which protection is sought. See also T0107/00: "indefinite feature is not rendered clear by functional features expressing the result to be achieved".

The non-compliance with the substantive provisions is to such an extent, that a meaningful search of the whole claimed subject-matter of the claims cannot be carried out (PCT Guidelines 9.19 and 9.23).

The compounds of formulas (I) and (IA) could be defined more precisely using the concrete definitions for the above mentioned variables, which do not represent an unduly restriction of the scope of the claims in view of the results put forward.

The Search Division considers the subject-matter of present claim 6 defining L 2, of claims 19-24 defining the moieties representing G/G1; of claims 52, 74, 75, 77 defining D1, L, D2 to represent a subject-matter on which a meaningful search could be performed since it represents a legitimated scope of protection in view of the examples and biological results put forward.

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2021/000813

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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