



(51) International Patent Classification:

C07K 14/71 (2006.01) C12N 15/113 (2010.01)

C07K 14/485 (2006.01) A61P 27/16 (2006.01)

(21) International Application Number:

PCT/US2020/063595

(22) International Filing Date:

07 December 2020 (07.12.2020)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/947,059 12 December 2019 (12.12.2019) US

(71) Applicant: **TING THERAPEUTICS LLC** [US/US];
9764 Ascot Dr., Omaha, NE 68114 (US).

(72) Inventors: **ZUO, Jian**; 9764 Ascot Dr., Omaha, NE 68114 (GB). **TEITZ, Tal**; 9764 Ascot Dr., Omaha, NE 68114 (US).

(74) Agent: **FENTRESS, Susan, B.**; Veritay Group IP, PLLC,
20 Dudley Street, Suite 601, Memphis, TN 38103 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ,

CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, 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.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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))

(54) Title: COMPOSITIONS AND METHODS FOR THE PREVENTION AND TREATMENT OF HEARING LOSS

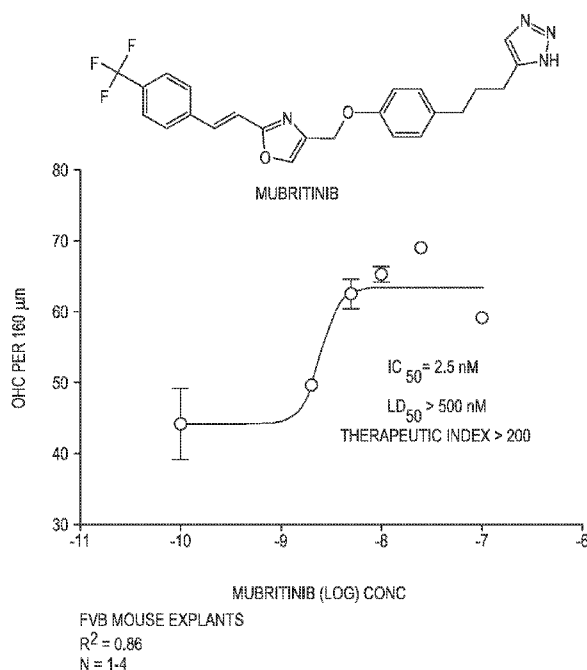


FIG. 1

(57) Abstract: Method, kit and pharmaceutical compositions using an inhibitor of EGFR signaling for prevention or treatment of hearing loss are described.

(88) Date of publication of the international search report:
05 August 2021 (05.08.2021)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/63595

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C07K 14/71; C07K 14/485; C12N 15/113; A61P 27/16 (2021.01)

CPC - C07K 14/705; C07K 14/185; C07K 14/4738; C12N 15/1138; A61P 27/16

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)

See Search History document

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

See Search History document

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	WO 2018/204226 A1 (ST JUDE CHILDREN'S RESEARCH HOSPITAL) 8 November 2018 (08.11.2018) para [0005], [0056], claims 1, 3, 4	1, 3, 4 ----- 2
Y	US 2019/0255090 A1 (JIANGSU MICROMEDMARK BIOTECH CO., LTD.) 22 August 2019 (22.08.2019) claims 6, 7	2

☐ 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

"D" document cited by the applicant in the international application

"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

4 May 2021

Date of mailing of the international search report

JUN 28 2021

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer

Lee Young

Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/63595

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.:
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:

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:

-----Go to Extra Sheet for continuation-----

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 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.:
Claims 1-4

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/US 20/63595

Continuation of Box III: Observations where Unity of Invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I+: Claims 1-10, drawn to a method where an inhibitor of EGFR signaling pathway is used for treatment or prevention of hearing loss.

The method of treatment or prevention of hair loss will be searched to the extent that the inhibitor is the first named, PAN-AUR inhibitor (claim 1), SNS-314 (claim 4). It is believed that claims 1-4 read on this first named invention and thus these claims will be searched without fee to the extent that they encompass SNS-314. Additional EGFR signaling pathway inhibitors will be searched upon payment of additional fees. Applicant must specify the claims that encompass any additional elected inhibitors. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be: B-raf inhibitor vemurafinib (claims 1-3, 8).

Group II: Claims 11-17, drawn to a pharmaceutical composition or kit comprising at least two inhibitors of EGFR signaling pathway.

The inventions listed as Groups I+ and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features:

Group I+ has the special technical feature of a method where an inhibitor of EGFR signaling pathway is used for treatment or prevention of hearing loss, not required by Group II.

Group II has the special technical feature of a pharmaceutical composition or kit comprising at least two inhibitors of EGFR signaling pathway, not required by Group I+.

Among the inventions listed as Groups I+ are the specific inhibitors of EGFR signaling disclosed within. Each invention requires a specific inhibitor not required by any other inventions.

Common Technical Features:

1. Group I+ inventions share the common technical feature of claim 1.
2. Groups I+ and II share the common technical feature of an EGFR signaling pathway inhibitor [comprised by claim 1]

However, said common technical features do not represent a contribution over the prior art, and are disclosed by WO 2018204226 A1 to St Jude Children's Research Hospital (hereinafter "SJCRH").

As to common technical features #1 and #2 [claim 1], SJCRH discloses use of an inhibitor of epidermal growth factor receptor (EGFR) signaling for the treatment of hearing loss, wherein the inhibitor of EGFR signaling inhibits the expression or activity (Claims 1 and 4; "1. A method for the treatment or prevention of hearing loss comprising administering to an animal in need thereof an inhibitor of epidermal growth factor receptor (EGFR) signaling"; "4. The method of claim 1, wherein the inhibitor of EGFR signaling inhibits the expression or activity of EGFR, Ras, Raf, MEK, ERK/MAPK, JAR, STAT, PI3K, AKT, mTOR, NCR, PAR, JNR, PLC, PRC or a cell cycle-associated protein kinase inhibitor").

As the common technical features were known in the art at the time of the invention, they cannot be considered common special technical features that would otherwise unify the groups. The inventions lack unity with one another.

Therefore, Groups I+ and II lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.