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(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT OF CANCER CHARACTERIZED WITH PCSK9 EXPRESSION

sgRNA1: 5' CATGCTTCATGTCACAGAGT 3'

sgRNA2: 5' TCATTTGACGCTGTCTGGGG 3'

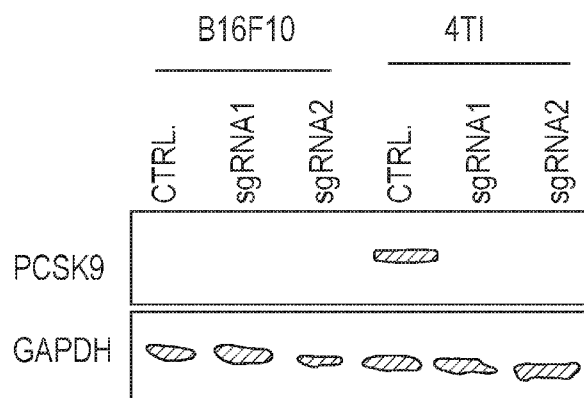


FIG. 1

(57) Abstract: A method for treating cancer in an individual comprises administering to the individual a therapeutically effective amount of a PCSK9 inhibitor. The method may further comprise administering to the individual at least one immune checkpoint inhibitor.





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))*

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

13 February 2020 (13.02.2020)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/38882

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 31/165, 31/7105, 39/00, 39/395, 45/06; C12N 15/113 (2019.01)

CPC - A61K 31/165, 31/7105, 39/00, 39/395, 45/06; A61P 35/00; C12N 15/1137

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	WO 2018/087391 A1 (INSERM, et al.) 17 May 2018; page 6, lines 5-8; page 16, lines 7-9; claim 4	1-2, 8-9
A	US 2013/0189278 A1 (MERCK SHARP & DOHME CORP.) 25 July 2013; entire document	1-2, 8-9
A	US 2018/0023071 A1 (PRONASCI INC.) 25 January 2018; entire document	1-2, 8-9

☐ 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

10 December 2019 (10.12.2019)

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02 JAN 2020

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US19/38882

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:

---Please See Supplemental Page---

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.:

1-2, 8-9; evolocumab antagonistic PCSK9 antibody (inhibitor); radiotherapy (additional treatment)

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
Information on patent family members

International application No.

PCT/US19/38882

-***-Continued from Box No. 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 examined, the appropriate additional examination fees must be paid.

Group I+, Claims 1-90, evolocumab antagonistic PCSK9 antibody (inhibitor), and radiotherapy (additional treatment) are directed toward method for treating cancer in an individual comprising: administering to the individual a therapeutically effective amount of a PCSK9 inhibitor.

The methods will be searched to the extent that they encompass an evolocumab antagonistic PCSK9 antibody (first exemplary inhibitor), radiotherapy (first exemplary additional treatment). Applicant is invited to elect additional PCSK9 inhibitor(s) and/or additional treatment(s) or additional specie(s) used for treatment (e.g. bispecific antibodies), where available as an option within at least one searchable claim, to be searched. Additional inhibitor(s) and/or treatment(s) or specie(s) used for treatment will be searched upon the payment of additional fees. It is believed that claims 1, 2 (in-part), and 8-9 encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass an evolocumab antagonistic PCSK9 antibody (inhibitor), and radiotherapy (additional treatment). Applicants must specify the claims that encompass any additionally elected inhibitor(s) and/or treatment(s) or specie(s) used for treatment (s). Applicants must further indicate, if applicable, the claims which encompass 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 conventional chemotherapy (additional treatment).

No technical features are shared between the inhibitors and/or treatments, of Groups I+ and, accordingly, these groups lack unity a priori.

Additionally, even if Groups I+ were considered to share the technical features including: a method for treating cancer in an individual comprising: administering to the individual a therapeutically effective amount of a PCSK9 inhibitor; a method for treating cancer in an individual comprising: administering to the individual a therapeutically effective amount of a PCSK9 inhibitor; and administering to the individual at least one immune checkpoint inhibitor; these shared technical features are previously disclosed by WO 2018/087391 A1 (INSERM, et al.) (hereinafter 'INSERM').

INSERM discloses a method for treating cancer in an individual (a method for treating cancer in an individual; claim 4) comprising: administering to the individual a therapeutically effective amount of a PCSK9 inhibitor (comprising: administering to the individual a therapeutically effective amount of a PCSK9 inhibitor; claim 4); a method for treating cancer in an individual (a method for treating cancer in an individual; claim 4) comprising: administering to the individual a therapeutically effective amount of a PCSK9 inhibitor (comprising: administering to the individual a therapeutically effective amount of a PCSK9 inhibitor; claim 4); and administering to the individual at least one immune checkpoint inhibitor (page 19, line 3; page 21, lines 3-4) .

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by a combination the INSERM reference, unity of invention is lacking.