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## (81) Designated States (unless otherwise indicated, for every

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(54) Title: COMPOUNDS FOR THE TREATMENT OF RETINITIS PIGMENTOSA AND METHODS OF MAKING AND USING THE SAME

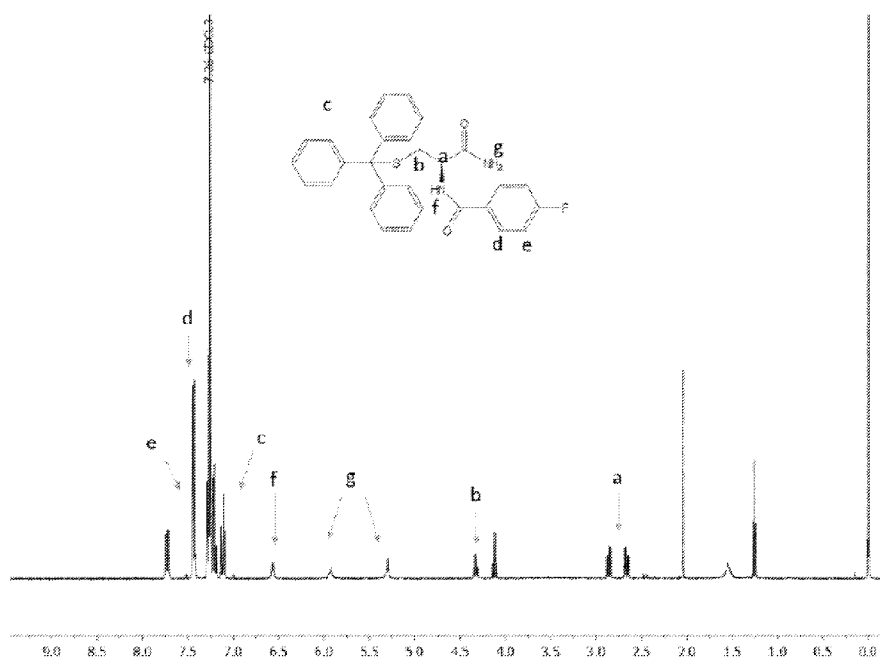


FIG. 1A

(57) Abstract: In one aspect, the disclosure relates to substituted N-acetylated cysteine- and selenocysteine-based compounds. Also disclosed are methods of making the same, pharmaceutical compositions comprising the same, and methods of treating eye disorders including retinitis pigmentosa (RP) using the same. In some aspects, the compounds can also have antimicrobial activity. This abstract is intended as a scanning tool for purposes of searching in the particular art and is not intended to be limiting of the present disclosure.



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, ME, 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).

**Declarations under Rule 4.17:**

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

**Published:**

- *with international search report (Art. 21(3))*

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

24 April 2025 (24.04.2025)

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/35948

## A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. A61K 31/16, C07C 233/01, C07C 233/18 (2024.01)

ADD. C07C 233/01 (2024.01)

CPC - INV. A61K 31/16, C07C 233/01, C07C 233/18

ADD. C07C 233/01

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         | PUBCHEM 388891440 deposited on 06 December 2019 (06.12.2019) pg. 1-5. Pg. 2, structure                                                                                    | 1;3;6                 |
| Y         |                                                                                                                                                                           | 9-12                  |
| Y         | US 11,173,135 B2 (THIOGENESIS THERAPEUTICS, Inc.) 16 November 2021 (16.11.2021)<br>Col 7, ln 44-51; Col 74, ln 50-54; Col 75, ln 4-5; Col 75, ln 20-22; Col 101, ln 60-62 | 9-12                  |
| A         | WO 2018/216823 A1 (TAISHO PHARMACEUTICAL, Co., Ltd.) 29 November 2018<br>(29.11.2018) ENTIRE DOCUMENT                                                                     | 1;3;6;9-12            |

☐ 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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

19 AUGUST 2024

Date of mailing of the international search report

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Name and mailing address of the ISA/US

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/35948

## 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:

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 1-12 directed to a compound represented by the structure of formula I. The compound will be searched to the extent that it encompasses the first species of a compound represented by the structure of formula I, wherein V is S, the stereochemistry at a carbon atom indicated by an asterisk is R or S; Y is a substituted alkyl; X is H, n is 0 and provided the analogue is not N-acetylcysteine amide or di-N-acetylcysteine amide. It is believed that claims 1, 3, 6 and 9-12 read on this first named invention, and thus these claims will be searched without fee. This first named invention has been selected based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines. Applicant is invited to elect additional compounds of claim 1, wherein each additional compound elected will require one additional invention fee.

\*\*\*\*\*CONTINUED IN SUPPLEMENTAL BOX III\*\*\*\*\*

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, 3, 6 and 9-12

### 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.

## CONTINUATION OF SUPPLEMENTAL BOX III: LACK OF UNITY

Applicants must specify the claims that encompass any additionally elected compound. 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. Additionally, an exemplary election wherein different actual variables are selected is suggested. An exemplary election would be the compound represented by the structure of formula I, wherein V is S, the stereochemistry at a carbon atom indicated by an asterick is R; Y is an alkyl; X is formula II, wherein, the stereochemistry at the carbon atom indicated by the double asterick is R, Z is substituted alkyl, n is 0, m is 0 and provided the analogue is not N-acetylcysteine amide or di-N-acetylcysteine amide (Claims 1,2,3,6, 8-12).

Group II: Claims 13-20 directed to a method for treating or preventing a disease or disorder of the eye in a subject, the method comprising administering to the subject N-acetylcysteine amide analog of any of claims 1-8 or a pharmaceutical composition of any one of claims 9-12 to the subject.

Group III: Claims 21-27 directed to a method for making the N-acetylcysteine amide analogue of any of claims 1-8, the method comprising steps (a) and (b).

The group of inventions listed above 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+ includes the technical feature of a unique compound represented by the structure of formula I, which is not required by any other invention of Group I+.

Group II includes the technical feature of a method for treating or preventing a disease or disorder of the eye in a subject, the method comprising administering to the subject N-acetylcysteine amide analog of any of claims 1-8 or a pharmaceutical composition of any one of claims 9-12 to the subject, which is not required by Groups I+ or III.

Group III includes the technical feature of a method for making the N-acetylcysteine amide analogue of any of claims 1-8, the method comprising steps (a) and (b), which is not required by Groups I+ or II.

## Common technical features:

The inventions of Group I+ share the technical feature of a compound represented by the structure of formula I which is not required for Groups II and III.

The inventions of Group II share the technical feature of a method for treating or preventing a disease or disorder of the eye in a subject, which is not required for Groups I+ and III.

The inventions of Group III share the technical feature of a method for making the N-acetylcysteine amide analogue of any of claims 1-8, the method comprising steps (a) and (b), which is not required for Groups I+ and II.

These shared technical features, however, do not provide a contribution over the prior art, as being anticipated PUBCHEM 388891440 (hereinafter "Pubchem"). Pubchem discloses an N-acetyl cysteine amide analogue having the structure according to formula I, wherein V is S, the stereochemistry is R, X is H; n is 0 and Y is alkyl and provided the analogue is not N-acetylcysteine amide or di-N-acetylcysteine amide (pg. 2, structure).

As said compound and compositions were known in the art at the time of the invention, these cannot be considered special technical features that would otherwise unify the inventions of Groups I+, II and III. The inventions of Group I+, II and III thus lack unity under PCT Rule 13.