

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference BCR-006WO		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US2024/019416	International filing date (<i>day/month/year</i>) 11 March 2024 (11.03.2024)	(Earliest) Priority Date (<i>day/month/year</i>) 09 March 2023 (09.03.2023)
Applicant BASECURE THERAPEUTICS LLC		

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. 1A



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. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed.
 - b. ☒ furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.1(a)),
☒ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.
3. Additional comments:

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.: **13-81**
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 examined, the appropriate additional examination fees need to be paid.

Group I+: claims 1-12 are drawn to double-stranded ribonucleic acids (dsRNAs) for inhibiting expression of Angiotensinogen (INHBE).

The first invention of Group I+ is restricted to an antisense strand selected to be SEQ ID NO: 598 and a sense strand selected to be SEQ ID NO: 589, and double-stranded ribonucleic acids (dsRNAs) for inhibiting expression of Angiotensinogen (INHBE) comprising the same. The 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. Specifically, the first named invention was selected based on the first listed element for each of the variables presented in the claims (see claim 1). It is believed that claims 1 and 3-12 read on this first named invention and thus these claims will be searched without fee to the extent that they read on SEQ ID NOs: 589 and 598.

Applicant is invited to elect additional antisense and sense strands, and their respective, corresponding, SEQ ID NOs to be searched in a specific combination by paying additional fee for each set of election. An exemplary election would be an antisense strand selected to be SEQ ID NO: 599 and a sense strand selected to be SEQ ID NO: 590, and double-stranded ribonucleic acids (dsRNAs) for inhibiting expression of Angiotensinogen (INHBE) comprising the same. Additional antisense and sense strands, and their respective, corresponding, SEQ ID NOs will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. 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.

The inventions listed in Groups I+ 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:

The Groups I+ formulas do not share a significant structural element, requiring the selection of alternative antisense and sense strands where "the dsRNA comprises a sense strand and an antisense strand each 15 to 30 nucleotides in length, wherein: (a) the antisense strand comprises a sequence that is at least 70% or 80%

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

identical to the sequence of SEQ ID NO: 598, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 589; (b) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 599, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 590; (c) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 600, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 591; (d) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 601, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 592; (e) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 602, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 593; (f) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 603, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 594; (g) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 604, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 595; (h) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 605, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 596; or (i) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 606, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 597” and where “the dsRNA comprises a sense strand and an antisense strand each 15 to 30 nucleotides in length, wherein: (a) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 616, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 607; (b) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 617, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 608; (c) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 618, and the sense strand a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 609; (d) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 619, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 610; (e) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 620, and the sense strand comprises a sequence that is at least 70% or 80% identical the sequence of SEQ ID NO: 611; (f) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 621, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 612; (g) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 622, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 613; (h) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 623, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 614; or (i) the antisense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 624, and the sense strand comprises a sequence that is at least 70% or 80% identical to the sequence of SEQ ID NO: 615.”

Additionally, even if Groups I+ were considered to share the technical features of a double-stranded ribonucleic acid (dsRNA) for inhibiting expression of Angiotensinogen (INHBE), wherein the dsRNA comprises a sense strand and an antisense strand each 15 to 30 nucleotides in length, these shared technical features do not represent a contribution over the prior art.

Specifically, WO 2023/003922 A1 to Alnylam Pharmaceuticals, Inc. (hereinafter, “Alnylam”) teaches a double-stranded ribonucleic acid (dsRNA) for inhibiting expression of Angiotensinogen (INHBE), wherein the dsRNA comprises a sense strand and an antisense strand each 15 to 30 nucleotides in length (Pg. 2, Lns. 10-16, the invention provides a double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of a metabolic disorder-associated target gene selected from the group consisting of inhibin subunit beta E (INHBE) ... wherein the dsRNA agent comprises a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15, e.g., 15, 16, 17, 18, 19, 20, or 21, contiguous nucleotides).

The inventions listed in Groups I+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.

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Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first 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 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, 3-12**

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.

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A. CLASSIFICATION OF SUBJECT MATTERIPC: **C12N 15/113** (2024.01); **A61K 31/713** (2024.01); **A61P 9/00** (2024.01)CPC: **C12N 15/1136**; **A61K 31/713**; **A61P 9/00**; **C12N 2310/11**; **C12N 2310/31**; **C12N 2310/321**; **C12N 2310/322**

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.
A	WO 2023/003922 A1 (ALNYLAM PHARMACEUTICALS INC.) 26 January 2023 (26.01.2023) entire document	1, 3-12
A	US 2007/0072175 A1 (COOPER et al.) 29 March 2007 (29.03.2007) entire document	1, 3-12
A	US 2022/0184114 A1 (REGENERON PHARMACEUTICALS INC.) 16 June 2022 (16.06.2022) entire document	1, 3-12
A	US 2004/0033493 A1 (TCHERNEV et al.) 19 February 2004 (19.02.2004) entire document	1, 3-12



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

“&” document member of the same patent family

Date of the actual completion of the international search

28 August 2024 (28.08.2024)

Date of mailing of the international search report

03 December 2024 (03.12.2024)

Name and mailing address of the ISA/US

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