PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing *(day/month/year)*	**19 APRIL 2007 (19.04.2007)**
Applicant's or agent's file reference P0701/BC/PCT	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/KR2007/001319	**17 MARCH 2007 (17.03.2007)**	17 MARCH 2006 (17.03.2006)

International Patent Classification (IPC) or both national classification and IPC

C12N 15/11(2006.01)i, A61K 48/00(2006.01)i

Applicant

BIONEER CORPORATION et al

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.
For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/KR	Date of completion of this opinion	Authorized officer
Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	19 APRIL 2007 (19.04.2007)	CHO, Kyung Joo Telephone No.82-42-481-8287

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/KR2007/001319

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established 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))

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:

   a. type of material
   - ☒ a sequence listing
   - ☐ table(s) related to the sequence listing

   b. format of material
   - ☐ on paper
   - ☒ in electronic form

   c. time of filing/furnishing
   - ☐ contained in the international application as filed.
   - ☒ filed together with the international application in electronic form.
   - ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additioanl copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-11	YES
	Claims	None	NO
Inventive step (IS)	Claims	1-11	YES
	Claims	None	NO
Industrial applicability (IA)	Claims	1-11	YES
	Claims	None	NO

2. Citations and explanations :

Reference is made to the following documents, which are also cited in the International Search Report.

D1: NCBI GenBank Accession No. NM_021975 (20 December 2003)
D2: Osteoarthritis Cartilage. 14(4):367-376 (22 December 2005)

1. Novelty (PCT Article 33(2))

The present invention relates to siRNA for inhibiting NF-kB/RelA expression, and medicine for medical treatment for rheumatoid arthritis comprising the same.

D1, which is considered to be the closest prior art, discloses a mRNA sequence of Homo sapiens v-rel reticuloendotheliosis viral oncogene homolog A, nuclear factor of kappa light polypeptide gene enhancer in B-cells 3, p65(avian) (RFLA), mRNA, which is made of 2444 nucleic acids.

Although the siRNA in claim 1 having one of the sequences ID No. 1 to 30 is partially the same as the sequence in D1, the length of the sequences in claim 1 and in D1 is different.

D2 also provides NF-kBp65-specific siRNA which inhibits the expression of genes of cyclooxygenase-2, nitric oxide synthase-2 and matrix metalloproteinase-9, that is paralleled with the initiation and progression of cartilage lesions in osteoarthritis model.

However, the siRNA sequences in claim 1 are not the same as those of D2(see Table 1).

Therefore, the subject matter of claim 1 and its dependent claims 2 to 5 is considered to be novel.

The subject matter of claims 6 to 11 is related to a medicine for medical treatment of rheumatoid arthritis which contains one of siRNAs in claim 1 or claim 5. Since the subject matter of claim 1 or 5 is considered to be novel as described above, the subject matter of claims 6 to 11, which are substantially referring to either claim 1 or claim 5, is also considered to be novel.

(Continued on Supplemental Box.)

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of :

Box. No.V.

2. Inventive Step (PCT Article 33(3))

In general, persons skilled in the art are considered to generate siRNA candidate by simply selecting a short sequence partially complementary to a known mRNA sequence. However, those skilled in the art would have to go through a much longer trial-and-error process in the laboratory to find a useful siRNA which can effectively inhibits the target mRNA, because all of the partial sequences are not considered to act as a useful siRNA. The same reasoning can be applied in claim 1, and the person skilled in the art is not considered to easily invent a useful siRNA in claim 1 from D1, even if the whole NF-kB mRNA sequence is disclosed in D1. In addition, the skilled person is not considered to easily invent siRNA in claim 1 from D2 or from the combination of D1 and D2, since the siRNA in claim 1 is completely different from that of D2, except that both are targeting NF-kB.

Therefore, the subject matter of claim 1 is considered to involve an inventive step, and that of claims 2 to 11, which are substantially referring to claim 1, is also considered to involve an inventive step.

3. Industrial Applicability (PCT Article 33(4))

Claims 1 to 11 have industrial applicability.