PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2017/050754	10.02.2017	11.02.2016

International Patent Classification (IPC) or both national classification and IPC
INV. A61K9/51 A61K9/00

Applicant
FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA

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 43*bis*.1(a)(i) with regard to novelty, inventive step and 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 usually 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 notifed the International Bureau under Rule 66.1*bis*(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.

Name and mailing address of the ISA:

European Patent Office
P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040
Fax: +31 70 340 - 3016

Date of completion of this opinion

see form PCT/ISA/210

Authorized Officer

Muller, Sophie

Telephone No. +31 70 340-0

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2017/050754

Box No. I Basis of the 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 sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

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

5. Additional comments:

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

1. Statement

Novelty (N)	Yes:	Claims	4, 7
	No:	Claims	1-3, 5, 6, 8-11
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11
Industrial applicability (IA)	Yes:	Claims	1-11
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Cited Documents

The following documents are referred to in this communication:

D1 US 6 663 881 B2 (KUNZ LAWRENCE L [US] ET AL) 16 December 2003 (2003-12-16)

D2 LÜTFI GENÇ: "Preparation and characterization of nocodazole-loaded solid lipid nanoparticles",
PHARMACEUTICAL DEVELOPMENT AND TECHNOLOGY,
vol. 19, no. 6, 10 September 2014 (2014-09-10), pages 671-676,
XP055309542,
US
ISSN: 1083-7450, DOI: 10.3109/10837450.2013.819017

D3 ROLANDO E. YANES, DERRICK TARN, NGELA A. HWANG, DANIEL P. FERRIS: "Involvement of lysosomal exocytosis in the excretion of mesoporous silica nanoparticles and enhancement of the drug delivery effect by exocytosis inhibition",
SMALL,
vol. 9, no. 5 , pages 697-704,

2. Clarity

The expression "inhibitor of exocytosis" used in claim 1 encompasses a large number of compounds which are defined only by reference to a desired functional activity, namely compound being an inhibitor of exocytosis. This functional term does not give a specific technical guidance for the selection of the suitable derivatives, without proven general knowledge, to show which derivatives are suitable "inhibitors" in the particular case of the current problem and thus could be seen as a mere invitation to the skilled person to perform a research program in order to find the suitable variants.

Therefore claim 1 lacks clarity, Article 6 PCT.

3. Novelty

D1 discloses (see column 4, line 46 - line 63; column 21, line 30 - line 60 and the claims) a therapeutic method comprising administering to a traumatized mammalian blood vessel a sustained release dosage form comprising biodegradable poly (DL-lactide-co-glycolide) nanoparticles having a size of 5 to 500 nanometers and comprising a cytoskeletal inhibitor, e.g., cytochalasin A,B or D. The sustained release dosage form comprising a cytochalasin is preferably administered via an implantable device which is not a catheter used to perform bloodless angioplasty.

The drug cytochalasin A,B or D is an inhibitor of exocytosis and an active ingredient.

The subject-matter of claims 1-3,5,6,8-11 is therefore not new in view of D1 (Article 33(2) PCT).

D2 discloses (see the abstract; page 671, column 2, line 8 - page 672, column 1, line 4; page 672; table 1; page 676, column 1, line 1 - line 11) Nocodazole-loaded solid lipid nanoparticles. Said nanoparticles are prepared using hot homogenization technique, which consists of:

i) forming a nanoemulsion comprising: a) 5% w/w nocodazole, b) 1,2% Tween 80, c) 5% Compritol (glyceryl behenate) and d) 90,8% water and

ii) obtaining solid lipid nanoparticles by recrystallization.

The drug nocodazole is an inhibitor of exocytosis and an active ingredient.

The subject-matter of claims 1-3,5,10,11 is therefore not new in view of D2 (Article 33(2) PCT).

4. Inventive Step

4.1. Not being new the subject-matter of claims 1-3,5,6,8-11 cannot be considered as inventive (Article 33(3) PCT).

4.2. Dependent claims 4 and 7 are not considered inventive in view of D1 and D2, insofar as they do not appear to comprise any technical features which lead to a non-obvious solution of a technical problem (Article 33(3) PCT).

5. Industrial applicability

Claims 1-11 satisfy the criterion of industrial applicability (Article 33(4) PCT).